



Obstetrics and Perinatal Death Review Committee (OPDRC) Substance Use Sub-committee

OPDRC Final Report
October 2025

Table of Contents

Membership.....	3
Acknowledgment.....	4
Introduction.....	4
Methodology	4
Case summaries.....	6
Socio-demographics.....	8
Health status and health care.....	10
Prenatal care.....	13
Details of the pregnancy	14
Substance use.....	15
Treatment for substance use	16
Scene details.....	17
Other factors.....	18
Discussion.....	19
Recommendations.....	23
Appendix A: Data collection tool.....	31
Appendix B: Literature Review.....	43
Appendix C: Case summaries.....	72
Appendix D: Summary of Risk Factors for Drug Toxicity in Pregnancy	75

Membership

Dr. Naana Afua Jumah

Member

Dr. Steven Bodley

Member

Kayla Baxendale

Member

Lisa Bishop RM

Member

Andi Camden PhD

Member

Jocelynn Cook PhD

Member

Dr. Laura Gaudet

Member

Jackie Girard RN

Member

Dr. Lisa Graves

Member

Brittany Groom RN

Member

Dr. Pamela Leece

Member

Jay MacGillivray RM

Member

Joy Nortei

Member

Dr. Alice Ordean

Member

Dr. Toby Rose

Member

Dr. Graeme Smith

Member

Dr. Suzanne Turner

Member

Mary-Elizabeth Vaccaro MSW

Member

Bekkie Vineberg RM

Member

Dr. Louise McNaughton-Filion

Committee Chair

Naomi Kasman MSc.

Epidemiologist Lead

Kristen Wong

Executive Lead

Acknowledgment

The subcommittee would like to acknowledge the individuals that are represented throughout this report and the loss experienced by their families, friends, and communities.

Introduction

The Obstetrics and Perinatal Death Review Committee (OPDRC) has been providing expertise to inform coroner investigations in Ontario since 1994. The committee goal is to identify individual and systemic factors affecting the health and safety of childbearing persons and newborns, make recommendations for improvements to decision-makers, as well as to inform families, professionals, institutions, and the public.

Similar to increasing substance toxicity trends seen in the general population, the OPDRC has observed an increase in the number of deaths from substance toxicity among pregnant and postpartum individuals. To gain additional perspective, the OPDRC initiated this subgroup focused on deaths in pregnancy due to accidental substance toxicity. This sub-committee brought together experts in public health, substance use intervention, obstetrical care, as well as persons with lived experience, with a common goal of reviewing these deaths to make recommendations to prevent further deaths.

Methodology

The OPDRC review of substance toxicity deaths in pregnancy comprised two phases: (1) a review of the literature to identify risk factors associated with substance toxicity in pregnancy, and (2) case reviews of unintentional acute substance toxicity deaths of pregnant individuals in Ontario.

Phase 1: Literature Review. A narrative literature review was conducted on the topic of "substance use and toxicity in pregnancy," with the goal of synthesizing literature on the epidemiology of substance use in pregnancy in Canada and identifying risk factors associated with substance toxicity in pregnancy. Results from this literature review informed the development of the OPDRC data collection tool ([Appendix A](#)) for subsequent use in the case reviews. Risk factors associated with substance

toxicity in pregnancy at the patient, provider, community, and system levels are summarized in tabular format in [Appendix D](#) and found in detail in [Appendix B](#).

Phase 2: Case identification and review. In Ontario, all non-natural deaths are investigated by a coroner, and all deaths, irrespective of manner, during pregnancy require investigation.

Searches were conducted on the coroner case management systems to identify deaths due to accidental acute substance toxicity in individuals who were pregnant. As no flag exists in the databases for identifying whether a deceased person was pregnant, a series of keywords were searched and the resulting case reports were individually reviewed to identify those where the person was pregnant at the time of death. Only accidental deaths were included (i.e., no suicides, homicides, or deaths with natural or 'undetermined' manner) and deaths related to chronic substance use – but not acute toxicity – were excluded. As well, deaths from trauma following substance use, such as motor vehicle collisions following the use of substances, were not included in this review.

Search criteria	
Manner of death = "Accident"	
Year of death between 2013 and 2022	
Death factor = "Acute alcohol or drug toxicity"	
Keywords:	
partum	pregnan
trimester	gestation
matern*	gravid
infant	baby
given birth	gave birth

Following the review of all deaths identified during the 10-year period between 2013 and 2022, a total of 18 deaths met the criteria for review by the OPDRC Substance Use subgroup. Brief summaries of the 18 deaths can be found in [Appendix C](#).

After the 18 deaths were identified in the coroner database, each death was the subject of a search of all Ontario Health Insurance Plan (OHIP) billings for each deceased person in the years prior to death, as well as records from the Ontario Narcotic Monitoring System. In addition, all hospital, paramedic, and police records,

if available, were seized under the coroner's authority for review. Post-mortem examinations, if performed, were included in the analysis and all other coroner reports were reviewed, containing social and personal history of the deceased. Medical records and coroner reports were further reviewed to determine if any other health care providers could be identified, and these records were obtained, if available. All information obtained was shared as a package with the reviewer assigned for that death.

Reviewers were clinicians, recruited from communities of practice with expertise in obstetrics and substance use treatment. An educational session was held for reviewers, prior to data collection, to demonstrate the OPDRC data collection tool ([Appendix A](#)) to help standardize data collection. After the reviews were completed, preliminary data and insights were shared with the committee as a whole, which included clinicians but also stakeholders and researchers in the health care of pregnant persons and those with lived experience, with effort to be geographically and culturally diverse in order to reflect the population of Ontario.

Recommendations were proposed and considered based on the group findings as a whole.

Case summaries

The time period for this review was the 10-year period between 2013 and 2022. In three of those years – 2014 to 2016 – there were no deaths due to accidental substance toxicity during pregnancy identified in the coroner database. Of the 18 deaths that were identified – for which case summaries are provided in [Appendix C](#) – half occurred in 2021-2022, with a steady increase in the number of deaths since 2019 (Figure A). While the absolute number of accidental substance toxicity deaths in pregnant persons each year is relatively low (ranging from zero to five per year), in 2022 these deaths represented 45% of all deaths among pregnant individuals (Figure B).

Figure A. Annual number and rate per 100,000 childbearing persons (i.e., females aged 10-49) of accidental substance toxicity deaths during pregnancy (N=18), Ontario, 2013-2022

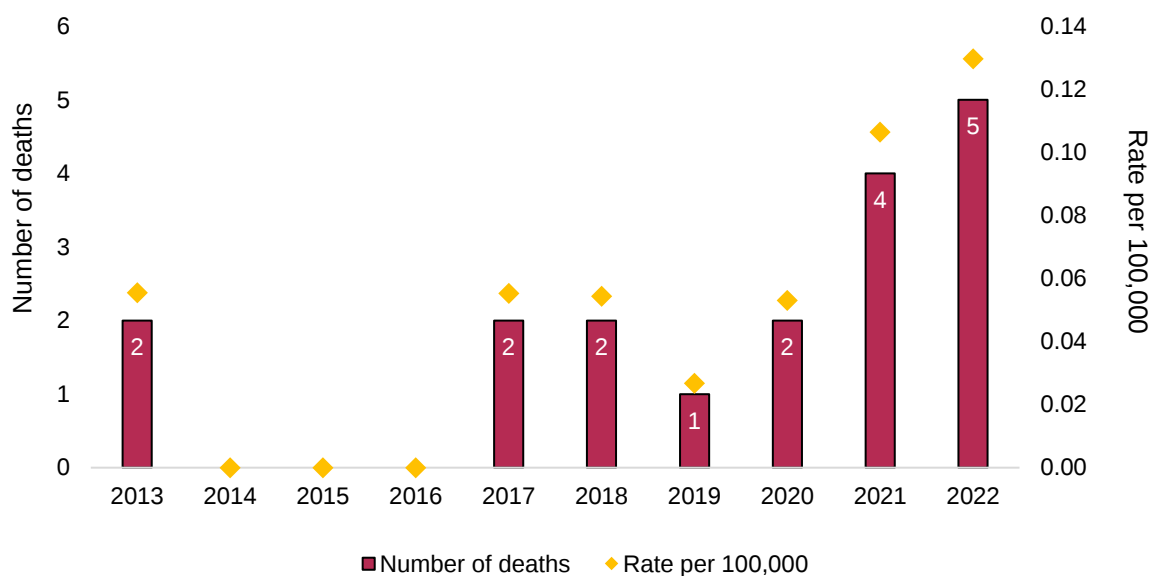
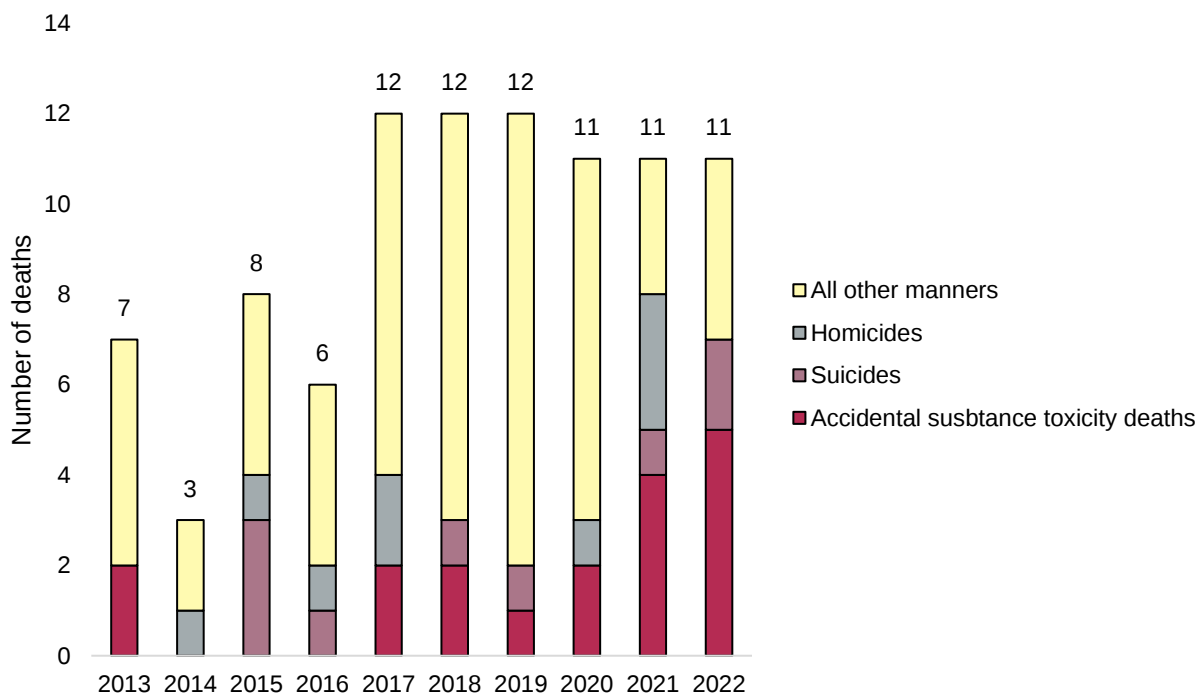
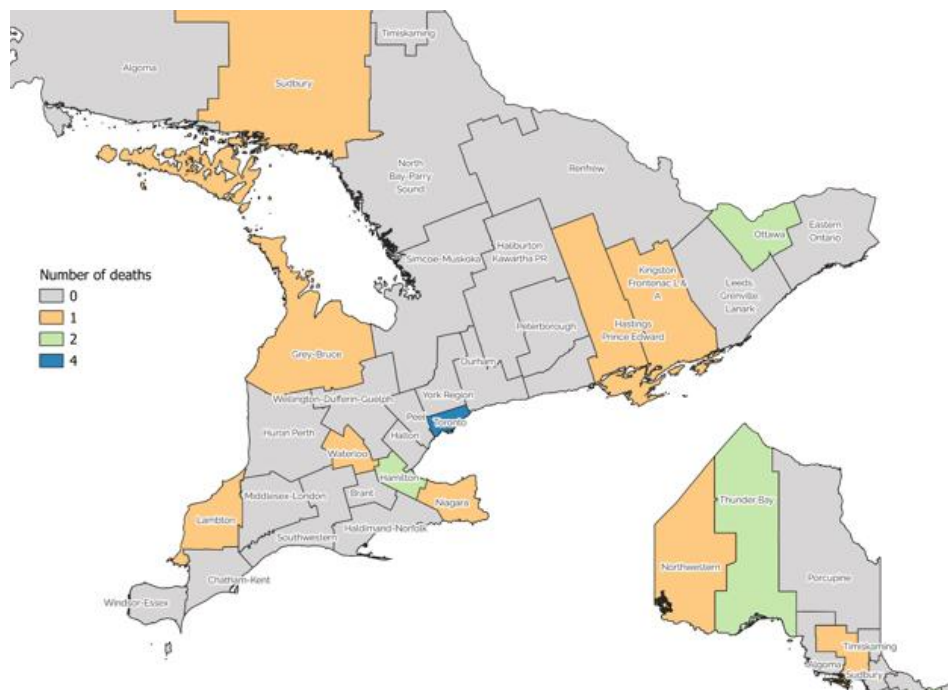


Figure B. Annual number of deaths during pregnancy by manner, Ontario, 2013-2022



The deaths reviewed by the committee occurred geographically across Ontario, occurring in 12 (out of 34) Public Health Unit (PHU) regions (Figure C). Only four of the PHUs – Hamilton, Ottawa, Thunder Bay, and Toronto – had more than one death in their region over the 10-year period. The Toronto PHU region saw four deaths during the time period.

Figure C. Map of 18 deaths during pregnancy due to accidental substance toxicity, by Public Health Unit, Ontario, 2013-2022



The age of the deceased persons varied greatly, ranging from 21 to 39 years (average 29 years), and the gestational ages at the time of death ranged from 4 to 36 weeks (average 19 weeks).

Socio-demographics

Information related to socio-demographic characteristics of the deceased individuals was accessed by the reviewers from reports prepared by the coroner at the time of death, which may include information provided during conversations with family and friends of the deceased, as well as documentation from interactions with the health care system. The completeness of this data is therefore dependent on how well the information was originally recorded. Also, since the information was

collected after death of the individual, information such as gender identity are not necessarily based on self-identification.

It is also important to note that much information was unknown or has been inferred. For example, reference to a "boyfriend" may have led reviewers to infer the decedent was unmarried and heterosexual. Similarly, whether someone who was engaged in sex work was defined as "employed" may not have been implemented consistently. While attempts were made to define these categories consistently, variation most likely occurred.

Within the context of the noted caveats, the socio-demographic information collected is presented in Table A (note: only response options that were selected are provided, refer to [Appendix A](#) for the full data collection form). 39% of the deceased individuals were single. One individual was known to identify as non-binary. While more than three-quarters of the deceased resided in a private dwelling, the remainder were unhoused or living in precarious living situations. Evaluation of the community where they resided at the level of material resource deprivation¹ - a metric that is closely associated with poverty - more than half resided in areas with the highest levels of material deprivation in the province.

Table A. Socio-demographic characteristics of those who died of accidental substance toxicity during pregnancy (N=18), Ontario, 2013-2022

	Number of deaths	Percent of deaths
Marital status		
Single	7	39%
Common-law	6	33%
Separated	1	6%
Unknown	4	22%
Gender		
Female	15	83%
Non-binary	1	6%
Unknown	2	11%
Sexual orientation		
Straight/heterosexual	12	67%
Pansexual	1	6%
Unknown	5	28%

¹<https://www.publichealthontario.ca/en/Data-and-Analysis/Health-Equity/Ontario-Marginalization-Index>

Citizenship		
Canadian	12	67%
Unknown	6	33%
Employment		
Student	1	6%
Employed	1	6%
Unemployed	9	50%
Unknown	7	39%
Rurality		
Large urban population centre	9	50%
Medium/small population centre	6	33%
Rural and non-metropolitan influenced zones	3	17%
Community level of material resource quintile¹		
1 – Lowest material resource deprivation	2	11%
2	0	0%
3	4	22%
4	2	11%
5 – Highest material resource deprivation	10	56%
Dwelling type and living arrangements		
Hotel/motel	1	6%
Private dwelling – living with family	10	56%
Private dwelling – shared accommodations	3	17%
Private dwelling – unknown arrangement	1	6%
Unhoused, in a shelter	1	6%
Unhoused, not in a shelter*	2	11%
Language(s) spoken		
English	18	100%

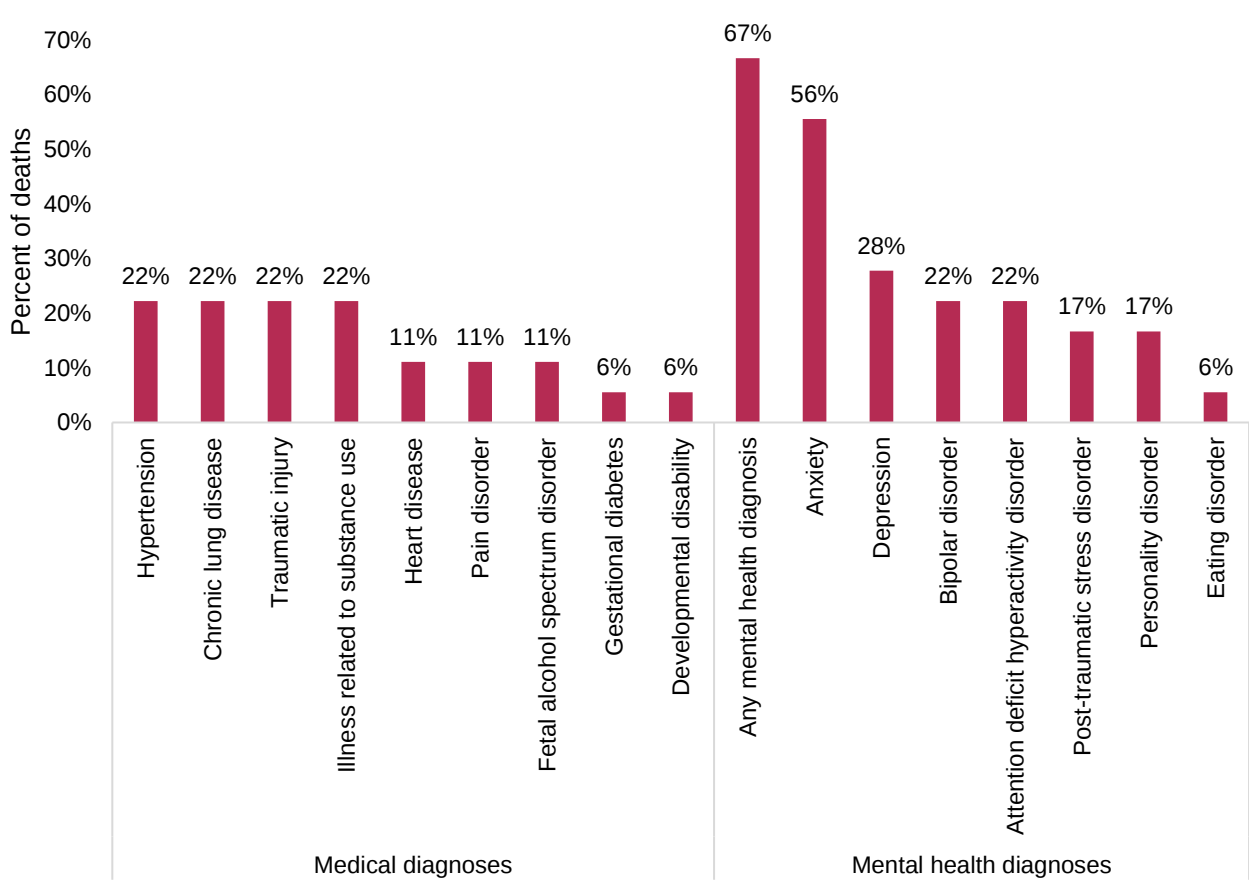
*Individuals who were "couch surfing" with friends or family are included in this category.

Health status and health care

In addition to reviewing the socio-demographics of the deceased individuals, a profile of their health status and access to health care was also created. Overall, just over half (56%) of the individuals were considered by reviewers to be attached to a primary care provider, such as a family doctor or nurse practitioner, who they could access for on-going medical care. The proximity or ease of access to a primary care provider is unknown, but records indicated that ongoing, consistent care was not common.

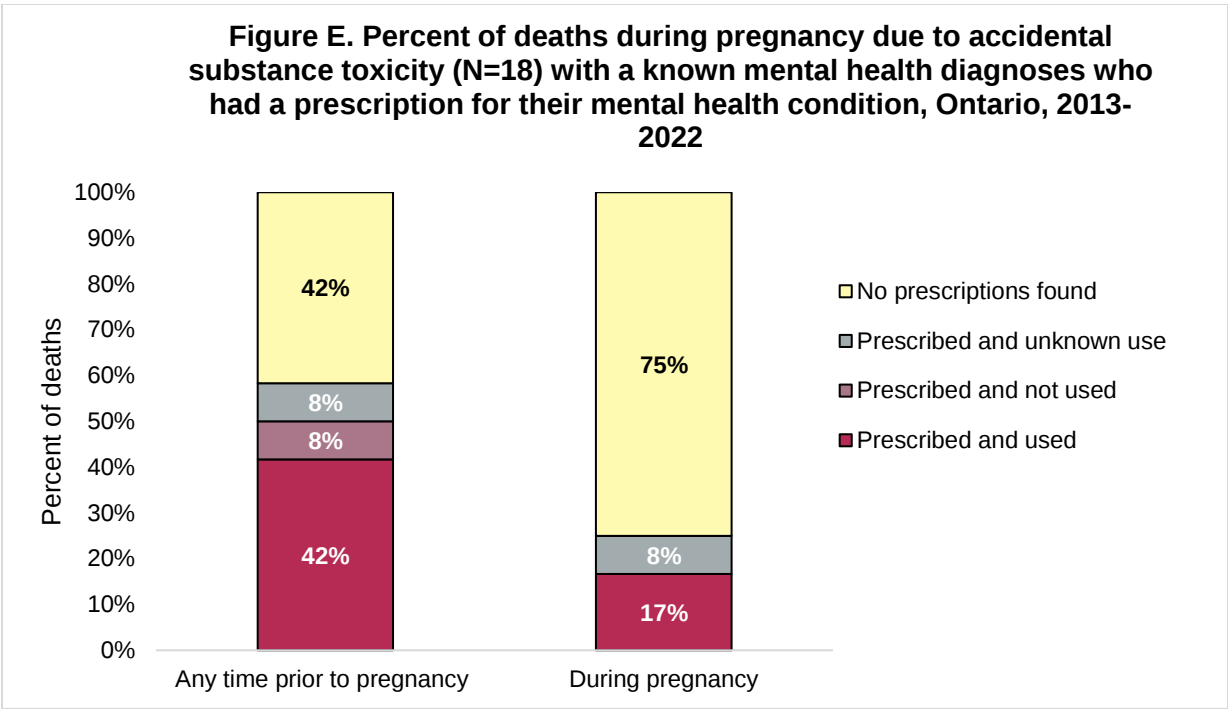
A wide range of medical diagnoses were identified for the deceased individuals, with the most common being hypertension (both gestational and non-gestational), chronic lung disease, traumatic injury, and illness related to substance use (Figure D). Mental health diagnoses were reported– in 10 out of 18 individuals –were anxiety, followed by depression. Overall, 12 out of 18 (67%) individuals had at least one mental health diagnosis. Given that many of the individuals may have not attended with a provider to receive an official diagnosis, the prevalence of these conditions is likely underestimated.

Figure D. Percent of deaths during pregnancy due to accidental substance toxicity (N=18) with select medical and mental health diagnoses, Ontario, 2013-2022



Despite the fact that two-thirds of the individuals had at least one mental health diagnosis recorded, 75% had no records of prescriptions for treatment of mental health conditions during pregnancy. 42% were known to have – and used – a prescription for a mental health condition prior to pregnancy compared to 17%

during pregnancy suggesting that a number of the deceased individuals may have stopped their prescriptions for a mental health condition while they were pregnant. While the reasons for stopping medication were largely unknown, active pregnancy may have been a factor.



Just over half (10) of the 18 individuals had at least one known interaction with the health care system during their pregnancy. The most commonly reported interaction was an emergency department (ED) visit (Table B). While information was not collected on the specific reason for the ED visit(s), reviewers noted that it was rarely related to the pregnancy, more frequently for issues related to substance use.

Table B also shows that 17% of the individuals had left a health care setting prior to being seen and 17% also had a patient-initiated discharge (i.e., left against medical advice). Arising from the review of the medical records, notes taken, and the services offered, at least four of the 18 individuals, appeared* to have experienced discrimination in their access to health care, for reasons including race, gender identity, and use of substances.

*Note: discrimination was an observation of the reviewer and not self-reported by any of the deceased persons.

Table B. Description of interactions with the health care system for individuals who died of accidental substance toxicity during pregnancy (N=18), Ontario, 2013-2022

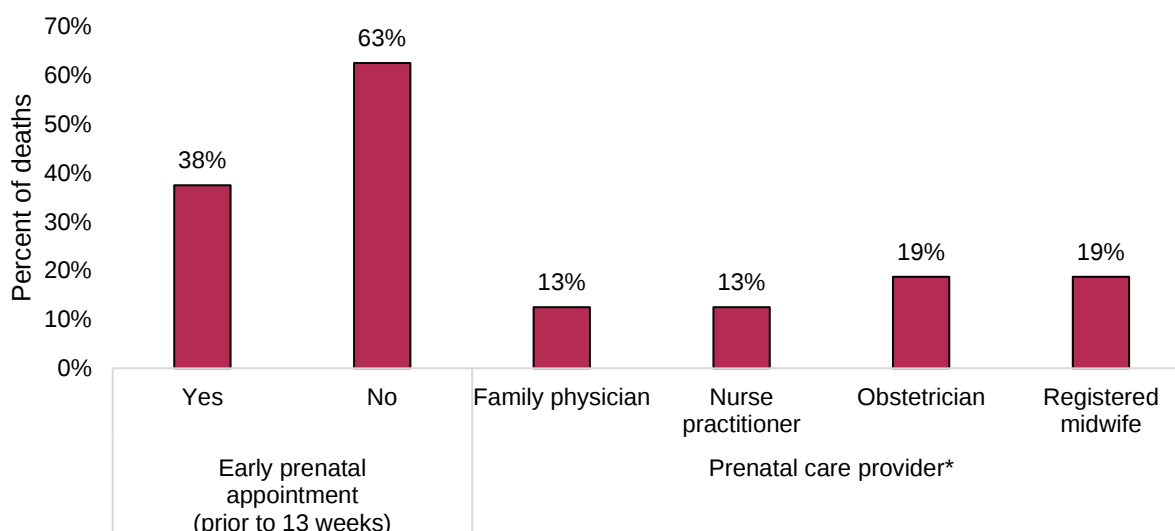
	Number of deaths	Percent of deaths
Health system interaction*	10	56%
Primary care visit	5	28%
Emergency department visit	8	44%
Specialist visit (including obstetrician)	3	17%
Other clinic (including midwifery)	2	11%
Left a health care setting without being seen	3	17%
Patient-initiated discharge	3	17%
Experienced discrimination when receiving health care	4	22%
Discriminated against due to race	1	6%
Discriminated against due to sex/gender identity	1	6%
Discriminated against due to substance use	2	11%

*Health system interactions are not mutually exclusive

Prenatal care

While the previous section discussed that 10 of the individuals had accessed some type of health care during their pregnancy, only eight had accessed reproductive health care and even fewer (three) had more than a single prenatal visit. It should be noted that two of the deaths occurred very early in the pregnancy (4-6 gestational weeks) and it was unclear if the deceased person had been aware they were pregnant at the time of death. Other details about the prenatal care received can be found in Figure F.

Figure F. Percent of deaths during pregnancy due to accidental substance toxicity (N=18) with an early prenatal appointment and by type of prenatal care provider, Ontario, 2013-2022



*Individuals may have seen multiple types of prenatal care providers and are counted towards each

Details of the pregnancy

While many individuals had limited (or no) prenatal care reviewers were able to access some information about the pregnancies shown in Table C. Pregnancy outcome included the majority of stillbirths and intrauterine deaths with a single live birth recorded. Additional information including where the person intended to deliver, whether the pregnancy was planned, and use of contraception was not available.

Table C. Description of pregnancy-related factors among those who died during pregnancy of accidental substance toxicity (N=18), Ontario, 2013-2022

Metric	Number of deaths	Percent of deaths
Pregnancy outcome		
Live birth	1	6%
Stillbirth/intrauterine death	15	83%
Neonatal death	2	11%
Type of pregnancy		
Planned	0	0%
Unplanned	5	28%
Unknown	13	72%
Type of contraception used		

Condoms	2	11%
IUD	3	17%
Unknown	13	72%
Manner to determine expected date of delivery		
T1 Ultrasound	4	22%
T2 Ultrasound	5	28%
Last menstrual period	1	6%
Unknown	8	44%
Location intended to deliver		
Level 1 Hospital	2	11%
Level 2 Hospital	1	6%
Unknown	15	83%

Substance use

Information was collected for each deceased person about substances they had used at any time, substances used during pregnancy, and those which contributed to death based on toxicology results (Table D). Fentanyl was the drug most frequently used during pregnancy (78% of individuals) and in all cases where it was used it contributed to the death of the individual. The next most commonly reported drugs used during pregnancy were methamphetamines (67%) and cocaine (44%) and, similar to fentanyl, in nearly all cases where these drugs were used, they contributed to the death of the individual.

Table D. Description of substances used by those who died during pregnancy of accidental drug toxicity (N=18), Ontario, 2013-2022

Substance	Ever used	Used during pregnancy	Cause of death*
Fentanyl	78%	78%	78%
Methamphetamine	67%	67%	61%
Cocaine	78%	44%	44%
Amphetamines	50%	33%	33%
Benzodiazepines	44%	11%	11%
Heroin	39%	6%	6%
Morphine	11%	6%	6%
Opioid (unspecified)	28%	6%	6%

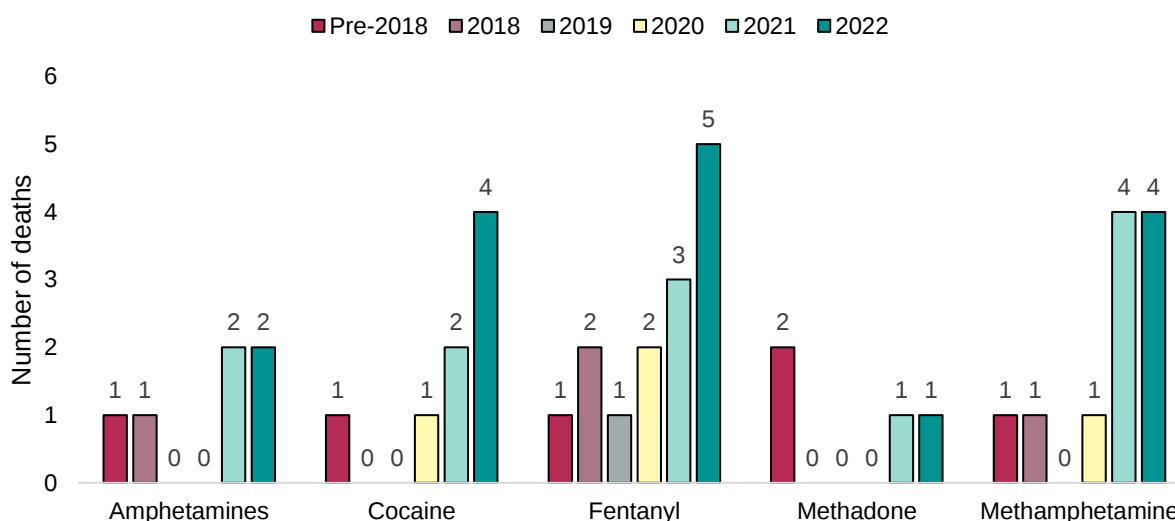
Alcohol	67%	17%	0%
Antipsychotics	6%	6%	0%
Hydromorphone	17%	0%	0%
Oxycodone	22%	0%	0%

*Cause of death may include multiple drugs for an individual that were each a causative agent in the death

In addition data collected showed that in 39% of cases there had been exposure to cannabis at some point during the pregnancy.

For a select group of five drugs, each of which contributed to more than two deaths in the cohort of cases reviewed their involvement in deaths over time is shown in Figure G. Although the numbers are small and trends must be interpreted with caution, there has been steadily increasing number of deaths associated with cocaine and fentanyl since 2019. Methamphetamines, saw an increase in substance-related deaths in 2021 and 2022.

Figure G. Number of deaths during pregnancy due to accidental substance toxicity (N=18), by involvement of drugs contributing to death, Ontario, 2013-2022



Treatment for substance use

Substance use predated pregnancy in all deaths reviewed. In the 12 (67%) deceased persons known to use substances for six or more years (and an additional five using substances for an unknown period of time) a variety of treatments had been accessed by these individuals, most before pregnancy occurred. 16 out of 18 individuals (89%) were known to have accessed at least one type of treatment for

substance use, and 12 out of 18 had accessed multiple treatments. The types of treatments are outlined in Table E.

The most common treatment was opioid agonist therapy (e.g. methadone and buprenorphine), with at least three individuals continuing methadone treatment into the pregnancy. One individual had access to harm reduction efforts – namely, supervised consumption and treatment service(s) – during pregnancy. Eight (44%) had undergone inpatient treatment prior to the pregnancy.

Table E. Description of substance-related treatments used by those who died during pregnancy of accidental substance toxicity (N=18), Ontario, 2013-2022

Treatment types*	Used – prior to pregnancy	Used – during pregnancy	Used – unknown timing
Any type of harm reduction	28%	6%	11%
Needle and syringe program			6%
Safer supply			
Supervised consumption	11%	6%	
Other	17%		6%
Any opioid agonist therapy	50%	17%	6%
Methadone	44%	17%	6%
Buprenorphine	22%		6%
Inpatient treatment	44%		
Other treatment	11%	6%	

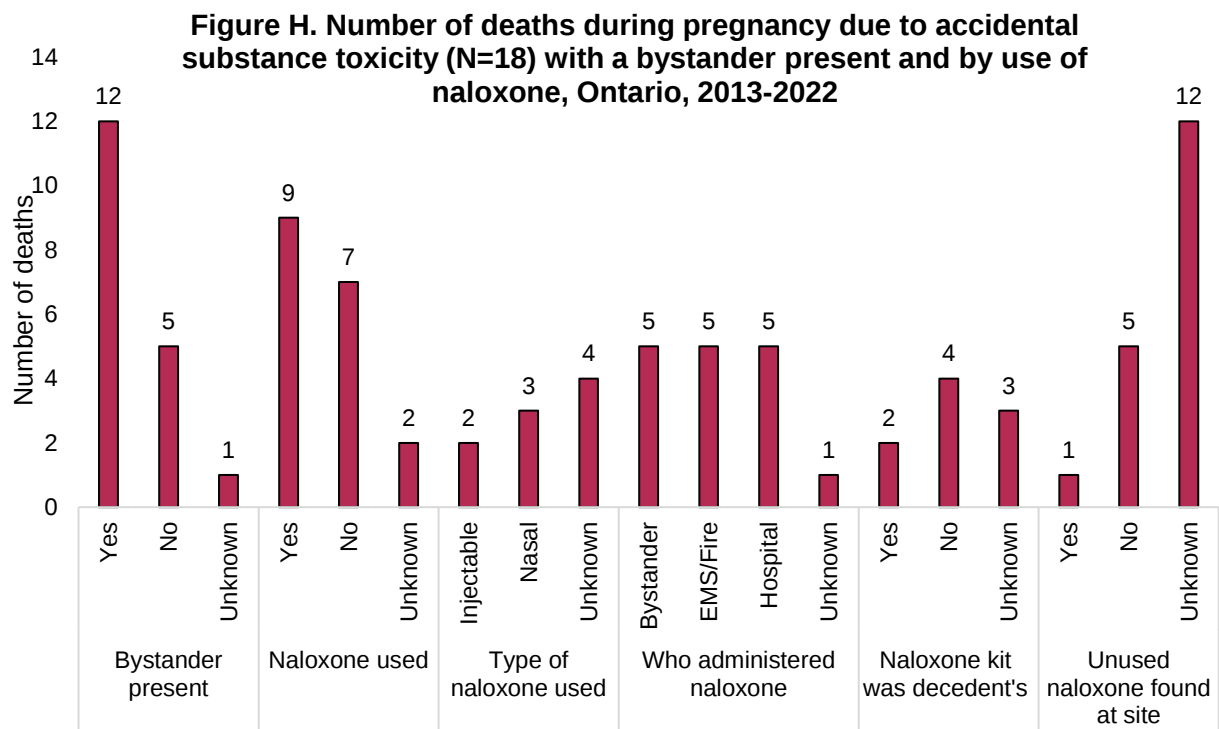
*Individuals may have accessed multiple treatments and are counted towards each

Scene details

Since 2018, the coroner information system expanded the information collected about the scene of death in acute substance toxicity cases, therefore, information prior to 2018 is more likely to be incomplete. When death occurred at home, a police report was sought and included in the information reviewed.

In two-thirds of the deaths reviewed there had been a bystander present which provided the potential for intervention following the toxicity incident (Figure H). Naloxone – which may temporarily reverse the effects of opioid toxicity – was administered in half of the cases. Naloxone was first made available to the public in Ontario in 2016. Naloxone needs to be administered quickly following a toxicity incident to be effective, so its lack of use in certain cases does not necessarily

identify a gap in resuscitation attempts, but possibly that the individual was not found until after the time for effective use of naloxone had passed.

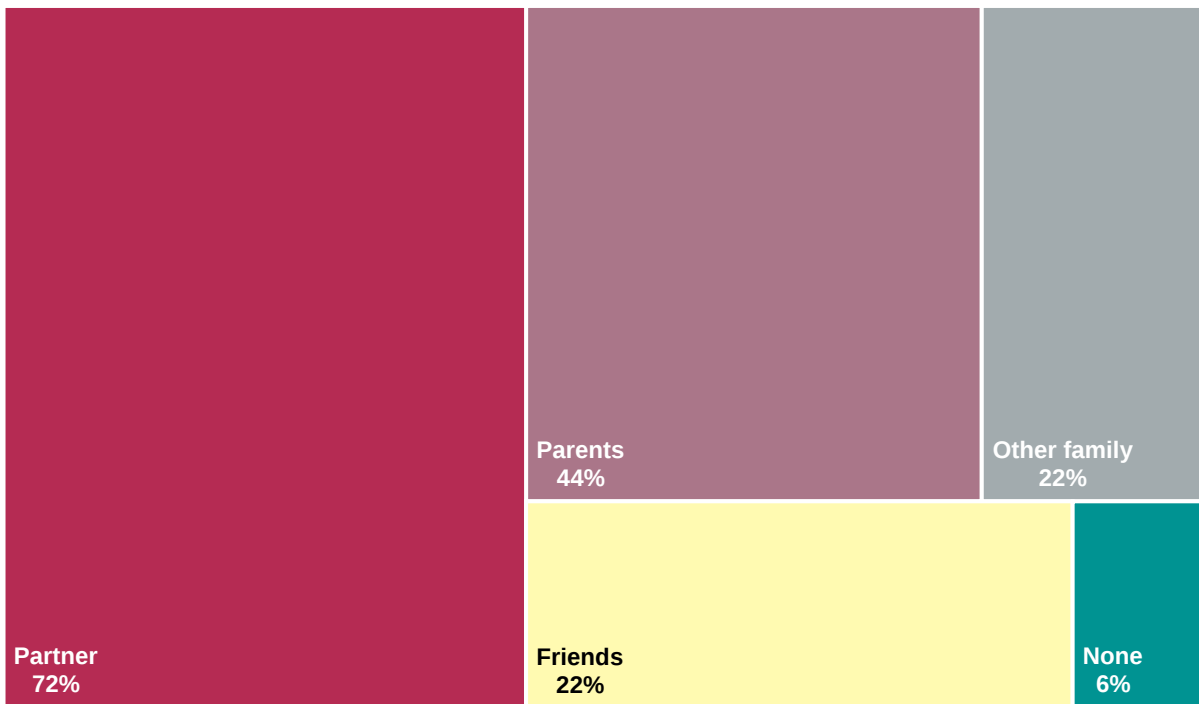


In five of the deaths, naloxone was administered by more than one individual or first responder. In two cases, the administered naloxone that was used belonged to the deceased person, and it was unknown if there was an unused naloxone kit at the site of the incident in two-thirds of the cases.

Other factors

The reviewers were asked to provide perspective about what type of social support network existed for each of the individuals--Figure I. All but one individual had a 'support', and in half of the cases more than one category was selected. It was most commonly reported that the partner of the individual was part of the person's support system, followed by the individual's parent(s).

Figure I. Types of support systems in place for those who died during pregnancy of accidental substance toxicity (N=18), Ontario, 2013-2022



In addition to their support system, other observations included 61% with a history of involvement with a child protection agency (either themselves or their children), 11% of individuals had been incarcerated at some point during their pregnancy, and 33% had experienced intimate partner violence.

Discussion

While the absolute number of deaths from substance use in pregnancy remain low, deaths have been increasing, accounting for 45% of all deaths among pregnant individuals in the last year studied (2022). Substance toxicity impacts persons of varied ages and at varying stages of pregnancy, with the majority of persons living in communities with the highest degree of material deprivation. As well, a substantial number of persons who died were precariously housed.

Although more than half of those who died of substance use in pregnancy had an identified primary care provider in their records, the most common access point for care during their pregnancy was the emergency department. Care was most often

provided for substance use or non-obstetrical issues in isolation, with pregnancy often not acknowledged or recognized.

Emergency departments are designed for episodic care. Although these individuals received episodic, emergency-based care, patient-centered ongoing care did not appear to be accessible or available for those using substances in pregnancy who presented to the emergency department. A “warm handoff” (direct care provider to care provider transfer of care) did not occur, and a group of persons with complex issues and minimal resources were often discharged to arrange their own follow up with a health care provider.

Without services that are easily available in the community for a pregnant person with substance use disorder, members of the expert review committee agreed that, with patient consent, a well-constructed inpatient substance use disorder program at a local hospital, taking into account pregnancy, could provide a pathway to holistic care following an emergency department encounter. If no local expertise is available, virtual assistance could be an appropriate option, to allow the person to stay in their own community and on discharge be linked to care close to home. This virtual assistance could help local care professionals provide a combined substance use and prenatal care.

The burden of illness was high in those who died from substances while pregnant. The individuals all had pre-existing substance use disorder as an identified illness, and died from the substances they reported using during pregnancy. In addition to substance use disorder, medical and mental health diagnoses were much more frequent in this group than in Ontarian persons within a similar age range².

Two thirds of those who died of substance toxicity in pregnancy had a mental health diagnosis, much higher than the average population³. During their pregnancy, a substantial number of persons appeared to have stopped taking prescribed medication for their mental health condition. Although many of these persons had

² Camden A, Ray J G, To T, Gomes T, Bai L, Guttman A. Prevalence of Prenatal Opioid Exposure in Ontario, Canada, 2014-2019. *JAMA Netw Open*. 2021;4(2):e2037388. doi:10.1001/jamanetworkopen.2020.37388

³ https://mdsc.ca/docs/MDSC_Quick_Facts_4th_Edition_EN.pdf

used opioid agonist therapy, harm reduction or other treatment for substance use disorder previously, use of these interventions was remarkably lower during pregnancy. The reason for this is not clear. Review of medical records did not indicate these persons were counselled to stop taking their medications or other treatment. Reasons for stopping medication or treatment, particularly in those who are socioeconomically disadvantaged, underhoused and without ongoing primary health care are multiple, but an active pregnancy may have been a factor.

In summary, these persons who died of acute substance toxicity in pregnancy were persons who had a higher health burden and concurrently limited access to ongoing health care, mental health, reproductive health and/or opioid agonist therapy, socioeconomic support and housing. A small number of those who died of substance use in pregnancy (11%) interacted with the justice system suggesting there is a need to review the importance of prenatal/reproductive health care and substance use treatment during incarceration.

It was encouraging to find that of all persons who died, only one had no identifiable personal support at the time of their death. 72% had a partner identified and many had parents or other family, or friends that were considered supports. With these supports identified, it may be beneficial in future death reviews to approach them directly (with next of kin consent) to seek their perspective, as well as community and care provider perspectives. Although coroner investigations often do include this information, this is usually not done in a structured manner. Members of the committee volunteered "Social autopsies"⁴ and the "Cradle Kalamazoo"⁵ initiative as structured templates to gather information from a social perspective, which could improve the quality of recommendations to prevent further deaths.

It was also recognized that 33% of those who died had experienced intimate partner violence and 61% intersected with a child protection service (either for themselves or their children). This information highlights the complex personal and societal issues confronting this at-risk group of people, and the need for holistic, trusting, trauma-

⁴ WHO-SEAJPH Vol 7 ISSUE 1_EDD_WITH DOIs+Cover.indd

⁵ <https://www.cradlekalamazoo.com/>

informed and supportive therapeutic relationships, taking into consideration existing support networks.

Overall, these eighteen substance toxicity deaths in pregnancy in the province of Ontario were highly preventable. After consideration of the circumstances, review of the literature and consensus from this multidisciplinary group, it is our sincere hope these recommendations will be implemented in a thoughtful and constructive way, to prevent further deaths and improve the health of childbearing persons and children in the future.

Recommendations

Please note, these recommendations were developed from information arising from the review of the 18 cases included in this review only.

To Ontario Health, Ministry of Health for Ontario, Health Canada:

1. Ontario Health, the Ministry of Health for Ontario, Health Canada should work with Ontario Public Health Units, Family Health Teams, Community Health Centres and the Ministry of Children, Community and Social Services to develop an evidence based, integrated, equitably funded “basket of care/services” that can then be used with a patient-centred focus to treat and support pregnant persons with substance use disorder.

The recipients of these recommendations should be guided by the principle that funded supports and services are provided to meet the unique prenatal and substance use health needs of First Nations, Inuit, and Métis persons on a distinction-based but substantively equal basis with non-Indigenous people.

a. This basket of care/services should be mandated to be available, easily connected to sites where the person seeks or is provided care (e.g. but not exclusively: hospital emergency department/labour and delivery, health care services in First Nations, Inuit, and Métis communities, substance use services, mobile outreach, midwifery group, supervised injection site, women's shelters, or transitional housing). They should be available 24/7 to allow for a “warm handoff” from one care provider to another.

b. This integrated care/service should be coordinated and linked to provide seamless care and support of the whole person during their childbearing years, including but not restricted to: prenatal care, primary and mental health care, sexual and reproductive health care, harm reduction/substance use disorder services, recovery, food security, parental support and housing.

c. Social services, an outreach/system navigator or a support person should be an integral part of this care, reflecting the needs of each

community and actively supporting individuals in their choice of and access to care. Part of their responsibility should be to raise awareness of the basket of services, through all points of contact within and outside the healthcare context.

d. These integrated services should be provided in consultation with the community, and persons with lived experience in substance use and pregnancy. Providers of care in communities should be part of the development process. A tenet of these services: persons using substances who are pregnant should not have to leave their communities to obtain care (e.g., substance use care concurrently with land-based or out in the country prenatal care)

e. Aspects of these integrated services should be mobile in nature, to reach persons where they are at the time of need, including their own residence, shelters or encampments. These integrated services should also be integrated into pre-existing health care delivery models, such as emergency medical services, family health teams, substance use services, emergency departments/ hospitals, inner city health providers and community health care centres.

f. Choice of services should be evidence-based, driven by the person receiving them, with the help of a navigator and not restricted by registration or financial agreements.

g. If all efforts are made for inclusive, culturally appropriate, trauma informed, non stigmatised care, and a person declines to engage in care, the person's autonomy should be respected and documented, with an "open door policy" for later care and support.

2. Ontario Health, the Ministry of Health for Ontario, Health Canada should work with Ontario Public Health Units and Canadian Research Initiative in Substance Matters (CRISM) to ensure sexual and reproductive health counselling and services, including pregnancy testing are available and provided in substance use services and emergency departments across the province. They should be tailored to the specific needs of a person with

substance use, as recommended by the Substance Abuse and Mental Health Services Administration (SAMHSA) and the Centre for Addiction and Mental Health (CAMH). Education and staffing flexibility may be required in these centres to achieve these goals.

Review committee note: Unfortunately, the majority of those who died of substance use toxicity in pregnancy did not regularly visit a primary care provider during their pregnancy, and no pregnancies were identified as planned amongst the persons who died. The most frequent site accessed for care appeared to be the emergency department, for non pregnancy related issues.

To the Office of the Chief Coroner (OCC) and Ontario Forensic Pathology Service (OFPS), Ontario Health Teams

3. The OCC and OFPS and/or Ontario Health Teams working with local public health substance use strategy groups should consider developing a "social autopsy" approach ([WHO-SEAJPB Vol 7 ISSUE 1 EDD WITH DOIs+Cover.indd](#)), particularly when reviewing a death of a pregnant person who has received little or no prenatal or other health care leading up to their death from acute substance toxicity. This may include, with the permission of the deceased person's family, interviews and discussions with family, the person's community, and care providers. These discussions should occur soon after the death, in order to better understand the circumstances and preventable factors that lead to the death, to better inform recommendations to prevent further deaths. The "Cradle Kalamazoo" initiative, which is based on collective action producing a collective impact, led by a local university and local public health in the USA, is another model which could be considered to address inequitable birth outcomes.

To Ontario Health, Canadian Association of Emergency Physicians (CAEP)

4. All persons of childbearing age presenting with possible substance toxicity should have BhCG testing as part of an order set in the emergency department.

Review committee note: The Ontario Health ED Pathways for Substance Use should include specific testing and care for persons of reproductive age (eg BhCG).

To Ontario Health, Ministry of Health for Ontario, Ontario Hospital Association

5. Ontario Health, the Ministry of Health for Ontario and the Ontario Hospital Association should encourage and develop local hospital pathways for admission of pregnant persons, to allow for expedited substance use and reproductive health care if no effective, accessible options are available in the community.

Within these local hospital pathways, a comprehensive order set should be available, ensuring pharmaceutical and supportive treatment with frequent reassessment of a person's condition. Expert guidance should be available to local hospital health providers virtually if there is no specialized service physically available. This virtual guidance should be adequately funded.

Consideration should be given to virtual substance use care using a similar treatment protocol in an outpatient/community/residence setting, which would be tailored to a person's/community's needs, culturally appropriate and without financial or geographical barriers.

Review committee note: When you need care for substance use, you need it immediately. Hospital based substance use care, in appropriate circumstances, can be a point of introduction to a full range of health and social supports. If housing is available and secure, it may be possible to provide virtual care outside of a hospital or institutional setting, with less perceived stigma.

To the Society of Obstetricians and Gynecologists of Canada, the Ontario Association of Midwives, the College of Family Physicians of Canada, the Royal College of Physicians and Surgeons of Canada

6. Sexual and reproductive health options should be discussed with patients during pregnancy or postpartum, including those with substance use, to address all pregnancy choices; reduce the risk of unplanned pregnancy and sexually transmitted infections.

To Ontario Health, Health Canada

7. Continuity of care and fragmentation of care occurs frequently when a pregnant person seeks care that may not be captured in the current medical databases. A Universal health care record should be easily available to health care providers, which would include midwifery and other reproductive health care, addiction medicine support, as well as primary care provider information. This Universal health care record should be easily available to all health care providers, with a patient's consent.

To Ontario Health, Ministry of Health for Ontario, Health Canada, Ontario Public Health Units, Family Health Teams, Community Health Centres, the College of Physicians and Surgeons of Ontario, the College of Midwives of Ontario, the College of Nurses of Ontario, the Ontario College of Pharmacists

8. All health care providers, including physicians, nurse practitioners, midwives and others providing primary care services should actively seek out health care information when caring for a person with substance use and pregnancy, and encourage their patients of childbearing age to consent to information release, whether or not a Universal health record is available. At the time of initial intake for those with substance use during childbearing age, a request should be made for consent to share information with other healthcare providers. Identification of a primary health care provider, a prenatal care provider, an addiction medicine provider and any mental health care provider should occur in any person of childbearing age. (Please refer to Recommendation #1, if no other health care providers are identified.)

To the Association of Faculties of Medicine of Canada, the Committee on the Accreditation of Canadian Medical Schools, the Canadian Association for Midwifery Education, the Canadian Association of Midwives, the Canadian Association of Schools of Nursing, the Canadian Nurses Association, the Council of Ontario Faculties of Medicine, the College of Family Physicians of Canada and the Royal College of Physicians and Surgeons of Canada

9. All organizations with a role in learner education in health professionals should make trauma-informed care a required part of the curriculum, ensuring this addresses substance use in pregnancy.

Equity, Diversity and Inclusion (EDI) training which addresses obstetrical issues should include a specific focus on Indigenous Health and the Truth and Reconciliation Commission of Canada: Calls to Action. Gender affirming care should be included.

To the Association of Faculties of Medicine of Canada, the Canadian Association of Midwives, the Canadian Nurses Association, the College of Family Physicians of Canada and the Royal College of Physicians and Surgeons of Canada

10. All healthcare providers should have knowledge about SBIRT (Screening, Brief Intervention and Referral to Treatment) or AAA (ask, assist and advise) for universal screening and intervening with pregnant persons (See recommendation # 9).

To Ontario Health, Ontario Pharmacists Association and Ontario College of Pharmacists, and Public Health Units of Ontario

11. Ontario Health, Ontario Pharmacists, Ontario College and Pharmacists and Public Health Units of Ontario should promote and provide easily accessible information, that naloxone should be used during pregnancy for a toxicity event.

Review committee comment: There were some instances in the cases reviewed, that naloxone was not provided by bystanders. The reasons for this are unclear. Ontario pharmacies and public health units may be able to explain the benefits of naloxone individually, with training, or via social media.

To Health Canada, the Ministry of Health for Ontario

12. There should be universal access (no cost) for any person who requires methadone, buprenorphine or other Opioid Agonist Therapy (OAT), such as what was made available in British Columbia in 2023 ([BC Gov News](#)).

13. All pregnant persons in Canada, including First Nations, Inuit, and Métis persons, should have universal access (no cost) to prescribed medications and non-prescribed essential prenatal medications, such as multivitamins, folic acid and ASA.

Review committee note: Many of the deceased had taken OAT or were prescribed mental health medication before pregnancy, with numbers dropping significantly for this when pregnant. Whether this was due to cost, the lack of a prescriber, or concerns about their impact on pregnancy is unknown, but cost as a barrier to appropriate treatment during pregnancy was highlighted many times.

To Accreditation Canada

14. Accreditation Canada should make the recognition and appropriate care for substance use in pregnancy, particularly in the emergency department, part of its key performance indicators related to substance use.

To the Office of the Chief Coroner/Ontario Forensic Pathology Service (OCC/OFPS)

15. The OCC/OFPS should consider identifying all pregnant persons in their database and performing a pregnancy test or equivalent testing in non-natural deaths of persons of childbearing age to improve the accuracy of data of deaths involving pregnant persons.

Review committee note: In the preparation for this review, some deaths during pregnancy were discovered that had not been identified as such in the coroner's database. During the review, it was noted that pregnancy was often not actively questioned or highlighted in substance toxicity deaths of persons of childbearing age. Members of the review committee noted that there was no automatic way to identify all pregnancy associated deaths for analysis. Some deaths in this review revealed that only the deceased person was aware of their pregnancy, despite it being, at times, relatively advanced. To ensure all deaths involving pregnancy are proactively identified, it would be helpful to have a "checkbox" or an automatic question of pregnancy/post partum status on persons of childbearing age, and a pregnancy test, if possible, on persons of childbearing age who die of non-natural

causes such as substance toxicity, particularly if dissection of the body is not planned or performed.

16. The OCC/OFPS should ensure distinction-based (First Nations, Inuit, and Métis) data are collected using OCAP principles (ownership, control, access and possession).

Appendix A: Data collection tool

OPDRC DATA COLLECTION TOOL

Case ID:

Residential postal code:

Postal code of incident:

DECEDENT FACTORS

Decedent's date of birth (dd/mm/yyyy)

Decedent's date of death (dd/mm/yyyy)

Sex: What sex was the decedent assigned at birth
(i.e., on the original birth certificate)

Gender identity: At the time of death, the decedent
considered themselves to be...

☐ Agender

☐ Man

☐ Non-binary

☐ Two-spirit

☐ Woman

☐ Unknown

☐ Other

Sexual orientation: At the time of death, the
decedent considered themselves to be...

☐ Bisexual

☐ Gay/Lesbian

☐ Straight/heterosexual

☐ Unknown

☐ Other

Marital status

☐ Common law

☐ Divorced

☐ Married

☐ Separated

☐ Single

☐ Widowed

☐ Unknown

Employment status at time of death

Type of housing

- ☐ Hotel/Motel
☐ Private dwelling
☐ Unhoused, living in shelter
☐ Unhoused, not in shelter
☐ Unknown
☐ Other

Living arrangements

- ☐ Lived alone
☐ Lived with family
☐ Lived in shared accommodations
☐ Other

What race category(ies) best describe this individual
(Select all that apply)

- ☐ First Nations
☐ Inuit
☐ Metis
☐ Black
☐ East Asian
☐ Latino
☐ Middle Eastern
☐ South Asian
☐ Southeast Asian
☐ White
☐ Unknown
☐ Other

Was decedent a Canadian citizen

If no, specify country of citizenship

What language(s) did the decedent speak
(Select all that apply)

- ☐ English
☐ French
☐ Other

Pre-pregnancy body mass index (BMI)

OR

Decedent's height (cms)

AND

Pre-pregnancy weight (kgs)

Number of pregnancies/gravidity (G)	
Number of previous term pregnancies (T)	
Number of previous preterm pregnancies (P)	
Number of previous stillbirths (S)	
Number of previous abortions (A)	
Number of living children (L)	

Additional comments or notes regarding DECEDENT FACTORS

HEALTH CARE AND SOCIAL SERVICES

Was the decedent attached to a primary care provider (e.g., family physician, nurse practitioner)

Relevant medical diagnoses
(Select all that apply)

- ☐ Acute or chronic illness related to substance use (e.g., cellulitis, endocarditis, hepatitis, HIV)
- ☐ Chronic kidney disease
- ☐ Chronic liver disease
- ☐ Chronic lung disease
- ☐ Diabetes (Type 1 or 2)
- ☐ Diabetes (gestational)
- ☐ Disability - developmental/intellectual
- ☐ Disability - physical
- ☐ Disability - sensory
- ☐ Disability - other
- ☐ Fetal Alcohol Spectrum Disorder
- ☐ Heart disease
- ☐ Pain disorder
- ☐ Sleep apnea
- ☐ Traumatic injury
- ☐ Other

Relevant mental health diagnoses
(Select all that apply)

- ☐ Anxiety
- ☐ Bipolar disorder
- ☐ Depression
- ☐ Eating disorder
- ☐ Schizophrenia
- ☐ Suicidal ideation/history of suicide attempts
- ☐ Other

Was the decedent prescribed/using any medication(s) for mental health conditions

	Prescribed and being used	Prescribed and not being used	Prescribed and unknown use	Unknown
Prior to pregnancy	☐	☐	☐	☐
During pregnancy	☐	☐	☐	☐

Provide any additional information regarding medications for mental health conditions prescribed and/or used by the decedent

Interactions with the health care system during pregnancy
(Select all that apply)

- ☐ Primary care visits
- ☐ Emergency/Urgent care visits
- ☐ Hospitalizations
- ☐ OAT clinics
- ☐ Specialist visits (e.g., obstetrics)
- ☐ Other

During the pregnancy, did the decedent leave any health care settings without being seen

During the pregnancy, did the decedent leave any health care settings against medical advice

List any health and social service agencies involved with the decedent

From your review of the files, do you believe the decedent experienced discrimination when receiving health care for any of the following reasons
(Select all that apply)

- ☐ Race, ethnicity, or skin colour
☐ Use of substances
☐ Immigration status
☐ Sexual orientation
☐ Sex or gender identity
☐ Religion
☐ Other

Additional comments or notes regarding HEALTH CARE AND SOCIAL SERVICES

FACTORS RELATED TO PREGNANCY

Pregnancy outcome

- ☐ Live birth
☐ Stillbirth/miscarriage
☐ Neonatal death

Type of pregnancy

- ☐ Planned
☐ Unplanned
☐ Unknown

Weeks pregnant at time of death
(Enter number between 1 and 44)

Days pregnant at time of death
(Enter number between 0 and 6)

OR

Expected date of delivery (dd/mm/yyyy)

Manner in which estimated date of delivery was determined

Contraceptive type last used

Unknown ☐

Month and year contraceptive use stopped
(mm/yyyy)

Location where decedent intended to give birth at the onset of labour

- ☐ Birth centre
☐ Home
☐ Hospital - Level 1
☐ Hospital - Level 2
☐ Hospital - Level 3
☐ Midwifery clinic
☐ Unknown
☐ Other

Number of fetuses

Type of conception

- ☐ Spontaneous
☐ Intrauterine insemination
☐ In vitro fertilization
☐ Unknown
☐ Other

If any assisted reproductive technology was used, indicate date of procedure (dd/mm/yyyy)

If IVF was used, indicate age of embryo at transfer

Did decedent have one or more prenatal appointment before 13+0 weeks gestation age

Total number of prenatal visits

Unknown

☐

If any prenatal visits, type(s) of provider(s) seen
(Select all that apply)

- ☐ Family physician
☐ Midwife - Registered
☐ Midwife - Indigenous
☐ Nurse practitioner
☐ Obstetrician
☐ Unknown
☐ Other

Additional details related to prenatal care

Smoking status history of decedent
(Select all that apply)

- ☐ Never
☐ Smoked/vaped prior to pregnancy
☐ Smoked/vaped during pregnancy
☐ Unknown

Did the decedent reside with a smoker

Was there cannabis exposure during pregnancy
(Used/tried cannabis at any point during this pregnancy in any form: smoked, vaped, eaten, topical, etc.)

Any specific problems with this pregnancy that should be noted

Any specific problems with previous pregnancies that should be noted

Additional comments or notes regarding FACTORS RELATED TO PREGNANCY

SUBSTANCE USE

Substances ever used

(Select all that apply)

- ☐ Alcohol
- ☐ Amphetamines
- ☐ Antipsychotics
- ☐ Benzodiazepines
- ☐ Cocaine
- ☐ Fentanyl
- ☐ Heroin
- ☐ Hydromorphone (e.g., Dilaudid)
- ☐ Methamphetamine
- ☐ Morphine
- ☐ Opioids (unspecified)
- ☐ Oxycodone
- ☐ Other

Substances used during pregnancy

(Select all that apply)

- ☐ Alcohol
- ☐ Amphetamines
- ☐ Antipsychotics
- ☐ Benzodiazepines
- ☐ Cocaine
- ☐ Fentanyl
- ☐ Heroin
- ☐ Hydromorphone (e.g., Dilaudid)
- ☐ Methamphetamine
- ☐ Morphine
- ☐ Opioids (unspecified)
- ☐ Oxycodone
- ☐ Other

Substances involved in death
(Select all that apply)

- ☐ Alcohol
- ☐ Amphetamines
- ☐ Antipsychotics
- ☐ Benzodiazepines
- ☐ Buprenorphine
- ☐ Cocaine
- ☐ Fentanyl
- ☐ Heroin
- ☐ Hydromorphone (e.g., Dilaudid)
- ☐ Methadone
- ☐ Methamphetamine
- ☐ Morphine
- ☐ Opioids (unspecified)
- ☐ Oxycodone
- ☐ Other

When did the decedent first start using substances

- ☐ No previous history of substance use
- ☐ <1 year
- ☐ 1 to 5 years
- ☐ 6+ years
- ☐ Unknown

Did the decedent have any previous non-fatal overdose(s)

If yes, number of previous overdoses

Describe circumstances of previous overdoses

History of treatment for substance use

	Before pregnancy ONLY	During pregnancy ONLY	BOTH before AND during pregnancy	Yes, timing unknown
Harm reduction - needle exchange	☐	☐	☐	☐
Harm reduction - safer supply	☐	☐	☐	☐
Harm reduction - supervised consumption	☐	☐	☐	☐
Harm reduction - other	☐	☐	☐	☐
Inpatient addiction treatment	☐	☐	☐	☐
Methadone	☐	☐	☐	☐
Buprenorphine	☐	☐	☐	☐
Other	☐	☐	☐	☐

For all treatments identified above provide any additional details, including other types of treatment, date of last treatment, length of time on treatment, dose information, changes to dosage, etc.

Was another individual present at the time of the incident/overdose who could intervene

Was naloxone used on the decedent

If yes, type of naloxone used
(Select all that apply)

☐ Injectable

☐ Nasal

☐ Unknown

If yes, number of times naloxone used Unknown ☐

If yes, who administered naloxone
(Select all that apply)

☐ Bystander

☐ EMS

☐ Fire

☐ Hospital

☐ Police

☐ Unknown

If yes, did naloxone kit belong to decedent

Were any unused naloxone kits found at the scene

Additional comments or notes regarding SUBSTANCE USE

OTHER CONTRIBUTING FACTORS

What personal support system was in place for the decedent during the pregnancy
(Select all that apply)

- ☐ Partner
- ☐ Parents
- ☐ Other family
- ☐ Friends
- ☐ None
- ☐ Unknown
- ☐ Other

Was the current pregnancy flagged to child protection agency (e.g., Children's Aid Society)

Was a child protection agency (e.g., Children's Aid Society) involved with the decedent prior to the current pregnancy

Was the decedent incarcerated at any time during the pregnancy

If yes, had they been released from a Correctional Facility within 4 weeks of death

Was there a history of domestic/intimate partner violence
(Select all that apply)

- ☐ Never
- ☐ Prior to pregnancy
- ☐ During pregnancy
- ☐ Unknown

Additional comments or notes regarding OTHER CONTRIBUTING FACTORS

--

SUMMARIZING THE NARRATIVE

Provide a brief summary of the circumstances leading to death in a narrative style

--

List any gaps or missed opportunities you've identified

(For example, Missed opportunity in ER where the decedent could have been referred directly to substance use treatment or prenatal care rather than discharged and asked to return)

--

Identify any specific issues that you feel are important to be addressed in the recommendations

(For example, The lack of comprehensive risk assessment at a person's first prenatal visit; Siloing of substance use and pregnancy in primary care/emergency care assessments)

--

Propose any recommendations you have, or who you feel recommendations should be directed to

--

Identify any records provided which may have been incomplete or where documentation could be improved. Please explain what was missing/needs improvement.

--

Additional case notes or comments

--

Appendix B: Literature Review

Substance Use and Toxicity Deaths in Pregnancy: A Literature Review

Andi Camden, PhD MPH and Jonathan Zipursky, MD PhD FRCPC

This document is produced pursuant to section 15 (4) of the Coroners Act, R.S.O. 1990, c. 37, on the basis that it is to be used for the sole purpose of a Coroner's investigation, and not for any litigation or other proceedings unrelated to the Coroner's investigation. Moreover, the opinions and summary expressed herein by the author do not take into account the specific facts and circumstances surrounding the deaths reviewed by the Expert Review Committee on Substance Use Deaths in Pregnancy.

Substance Use and Toxicity Deaths in Pregnancy: A Literature Review

Background

Drug toxicity (poisoning from unregulated or prescribed drugs) is a leading cause of pregnancy-associated deaths (deaths in pregnancy or within one-year of the end of pregnancy) in the United States (US).^{1,2} Drug toxicity-related deaths in pregnancy reached record highs in the US following the onset of the COVID-19 pandemic.^{1,3} From 2017 to 2020, mortality from drug toxicity increased from 6.6 to 11.9 deaths per 100,000 live births in the US, which represents an 81% increase.¹ Rising mortality rates are attributed to increasing prenatal substance use, the drug toxicity crisis, contamination of the unregulated drug supply with more potent, synthetic opioids and stimulants, increased perinatal mental illness, and limited access to healthcare in pregnancy and the postpartum period.^{1,4,5} While similar Canadian mortality data are not yet available, there have been significant increases in substance use in pregnancy and drug toxicity.⁶⁻⁹ These trends are concerning and have important implications for maternal and child health.

Prenatal substance use can lead to maternal and child health complications through several mechanisms, including physiologic, socio-environmental, and clinical factors. Most substances, such as alcohol, cannabis, stimulants, and opioids, cross the placenta and can have adverse impacts on the developing fetus, including changes in brain structure, size, and function.¹⁰⁻¹² Prenatal substance use often occurs among people with low socio-economic status (e.g., residing in deprived areas, low income, low levels of education), social disadvantage (e.g., homelessness, exposure to violence, child welfare involvement, racism, sexism, criminalization), co-occurring medical conditions (e.g., mental illness, chronic pain), and clinical factors (e.g., lack of access to healthcare, delayed/no prenatal care).¹³⁻¹⁷ The intersection of these factors can compound adverse health outcomes.

Substance use in pregnancy is associated with perinatal health complications (e.g., stillbirth, preterm birth, intrauterine growth restriction, neonatal abstinence syndrome [NAS]) and poor maternal (e.g., infection, mortality) and child health (e.g., neurodevelopmental concerns, mortality) outcomes.¹⁸⁻²² Additionally, people who use drugs in pregnancy experience barriers to care, including stigma, discrimination, fear of child welfare involvement, limited access to care for those living in rural/remote areas, and lack of transportation and childcare.^{23,24} Prevention and treatment efforts must address these, and other structural and system-level barriers to care.

Detailed information on substance use and drug toxicity in pregnancy can inform prevention and treatment efforts. Incidental and unintentional deaths, including drug toxicity, have been excluded from measures of maternal mortality and maternal death reviews.²⁵ Further, Canada does not have a standardized national system to collect information on maternal deaths. As a result, little is known about the circumstances, socio-environmental, and clinical factors associated with substance-related deaths in pregnancy. To address these knowledge gaps, we conducted a narrative literature review to describe the epidemiology of substance use in pregnancy, and characteristics and risk factors associated with drug toxicity in pregnancy. Findings from this review will: 1) direct an obstetric and perinatal death review of unintentional substance use-related deaths in pregnancy in Ontario, and 2) inform recommendations to prevent drug toxicity and maternal deaths.

Evidence Used in This Review

We performed a narrative literature on the topic of “substance use and toxicity in pregnancy,” with the goal of synthesizing literature on the epidemiology of substance use in pregnancy in Canada and identifying risk factors associated with drug toxicity in pregnancy. We searched PubMed, Google Scholar, and Google from inception to February 2024 using combinations of the terms “alcohol,” “substance,” “drug,” “cocaine,” “opioid,” “cannabis,” “stimulant,” “meth*,” “benzo*,” “pregnan*,” “prenatal,” “antenatal,”

“maternal,” “overdose,” “toxicity,” “poisoning,” “death,” “mortality,” “risk,” “factor,” “determinant,” “predictor,” and “Canada.” We included English-language studies and focused on the most recent, Canadian studies (where available).

Epidemiology of Substance Use in Pregnancy

This section presents the epidemiology of the most commonly used substances in pregnancy, including prevalence, temporal trends, and maternal characteristics, where available. While individual substances are described below, it should be noted that polysubstance use is common among people who use drugs in pregnancy, and importantly, increases the risk of drug toxicity.^{1,26-28}

Alcohol

National surveys show that 9.9% of pregnant Canadians report consuming alcohol.^{29,30} In contrast, birth registry data in Ontario suggest approximately 2% of pregnant people report consuming alcohol, with rates up to 6.8% in rural/remote areas.³¹ The prevalence of alcohol use in pregnancy in Ontario has remained stable from 2013 to 2021.³¹ People who consumed alcohol in pregnancy were more likely to be older (≥ 35 years), White race, employed, married, have a post-secondary degree, and report smoking in pregnancy and binge drinking in the year before pregnancy.²⁹

Cannabis

In a population-based study of over 700,000 live and stillbirths collected through a birth registry in Ontario, self-reported cannabis use in pregnancy ranged from 1.2% in 2012 to 1.8% in 2017.¹⁶ In October 2018, changes in Canadian legislation allowed the consumption, sale, and distribution of cannabis for non-medical use.³² Following legalization, self-reported cannabis use in pregnancy was 4.2% in Ontario in both 2020 and 2021, with rates up to 17.5% in rural and remote areas of Ontario. Moreover, a

recent population-based study showed that cannabis-related acute care visits in pregnancy nearly doubled following cannabis legalization.³³ The highest rates of prenatal cannabis use were in people ages 15-24 years, living in low-income and rural areas, and among those who reported consuming alcohol and smoking in pregnancy.¹⁶ Similarly, in a population-based study of 1,280,447 singleton births in British Columbia, Ontario, and Newfoundland and Labrador, 2% of people reported prenatal cannabis use; 55.0% also reported prenatal tobacco use, 13.6% reported prenatal alcohol use, and 13.1% reported other prenatal substance use (i.e., opioids, cocaine, solvents).²¹

Opioids

Opioid use in pregnancy has increased substantially over the past two decades. There are several indicators of increasing prenatal opioid use in Ontario over the past two decades. There has been a 15-fold increase in NAS from 0.28 to 4.29 per 1000 live births from 1992 to 2011,⁸ and a 16-fold increase in the number of births among women with opioid use disorder who were public drug plan beneficiaries (46 in 2002 to 761 in 2014).³⁴ Self-reported estimates from birth registry data suggest approximately 1.1% of births in Ontario had prenatal opioid exposure, ranging from 1.3% in 2012-2013 to 1.1% in 2017-2018.²⁰ However, estimates based on linked administrative data show that birth registry data likely under-estimate prenatal opioid use. Using a combination of maternal and newborn hospital records, outpatient physician visits, and prescription opioid records, approximately 5.3% of hospital births in Ontario from 2014 to 2019 involved prenatal opioid exposures.¹³ Recent trends show decreases in prenatal opioid analgesic use from 2014 to 2019, likely reflective of revised opioid prescribing practice guidelines to promote safer prescribing and increased recognition of opioid-related harms. However, rates of treatment for maternal opioid use disorder (OUD), neonatal abstinence syndrome (NAS), and maternal opioid-related hospital care remained stable.¹³ People who use opioids for pain management in pregnancy are more likely to have medical comorbidities (including chronic pain conditions and psychiatric disorders), higher pre-pregnancy body mass index, to be ≥ 35 years old, and have a low household income.^{14,19,35-37} In contrast, people who have opioid use disorder or

unregulated opioid use in pregnancy are more likely than people who do not use opioids to have low socio-economic status, social instability (e.g. violence, homelessness, infant apprehension to social services, poverty), and high rates of co-occurring mental illness, chronic medical conditions, and polysubstance use.^{14,26,38-41} For example, among people with opioid use in pregnancy with high social and medical needs in Ontario, 55% had hospital care for mental illness, 52% had non-opioid drug-related healthcare use, and 38% had alcohol-related healthcare use in the two years before pregnancy.¹³

Stimulants

Stimulant use in pregnancy, particularly methamphetamine use, is an emerging public health concern. Rates of stimulant use and toxicity in pregnant are increasing globally.^{17,42} In a population-based analysis of 144,779 live births in British Columbia between January 1, 2015 and March 31, 2018, 0.7% of births had prenatal exposure to cocaine and 0.5% had prenatal exposure to 'other drugs,' including hallucinogens and stimulants (e.g., methamphetamine).⁴³ Similarly, US estimates of prenatal methamphetamine use are between 0.25% and 0.7%.^{42,44} Pregnant people with methamphetamine use tend to be younger (<24 years of age), White race, have diagnosed mental illness, low socio-economic status, and an increased risk of involvement with the criminal justice system.¹⁷

Non-specific substance use

Non-specific substance use includes prenatal use of street drugs and inappropriate use of prescription and non-prescription drugs and excludes alcohol use. Birth registry data for Ontario suggest the prevalence of self-reported drug use (including cannabis) in pregnancy was 1.9% in 2013 and 2.6% in 2018, with rates up to 14.3% in 2018 in rural/remote areas of Ontario.⁴⁵ More recent estimates from 2020 and 2021 (excluding cannabis use) show 1.0% of pregnant people in Ontario reported substance use in pregnancy, with rates as high as 9.4% in rural/remote areas.⁴⁵

Drug toxicity in pregnancy

Few Canadian data exist on the prevalence and characteristics of unintentional drug toxicity and death in pregnancy. The Public Health Agency of Canada provides data on non-fatal and fatal hospitalizations from drug toxicity in pregnancy. These data show a 2-fold increase in the number of drug toxicity hospitalizations in pregnancy from 31 in 2009 to 62 in 2021.⁷ Almost half (47%) of these events were classified as unintentional. Opioids are the most commonly involved substances implicated in severe drug toxicity in pregnancy. Opioids were involved in 89% and 71% of drug toxicity hospitalizations in 2021 and 2022, respectively.⁷

The all-cause maternal mortality rate in Canada increased from 3.1 to 8.0 per 100,000 live births between 2000 and 2022.⁴⁶ However, this rate may be an under-estimate due to underreporting.²⁵ Substance use contributed to 21.8% of maternal deaths in pregnancy, or within one-year of the end of pregnancy, in Canada from 2013 to 2017.⁴⁷ The contribution of substance use to pregnancy-associated deaths in Ontario is lower than national estimates. Of the 273 pregnancy-associated deaths from 2004 to 2020 in Ontario, 13.3% were attributed to drug toxicity.⁴⁸ Similarly, in Alberta, 12% of pregnancy-associated deaths from 1998 to 2015 were attributed to drug toxicity; decedents were <35 years of age, 83.3% smoked in pregnancy, 27.8% were prescribed psychiatric medications, and 21.7% had a psychiatric diagnosis.⁴⁹ In contrast, recent US estimates from 2020 show pregnancy-associated drug toxicity mortality rates are 11.9-13.4 deaths per 100,000 live births.^{1,3}

Groups disproportionately affected by prenatal substance use

First Nations groups are disproportionately impacted by prenatal substance use in Ontario. Differences in patterns of substance use are rooted in colonialism, intergenerational trauma, and disparities in access to care and treatment for substance

use disorders.^{50,51} For example, rates of opioid use in pregnancy are higher among Indigenous peoples in Canada compared to non-Indigenous people.^{50,52,53} One-third of all pregnant people on medication for opioid use disorder in Ontario are First Nations.⁵⁰ A recent report co-created by the Chiefs of Ontario and ICES showed 16% of First Nations peoples had significant prenatal opioid use with rates up to 31% in northwestern Ontario.⁵⁰ Most residents in northwestern Ontario are First Nations people living in rural and remote communities. Births with prenatal opioid exposure in this area have high rates of co-exposure to maternal tobacco (up to 89%), polysubstance (up to 54%), and alcohol use (up to 26%).⁵⁴

People with intellectual/development disabilities also have higher rates of substance use compared to people without disabilities.⁵⁵ This disparity stems from features of the disability, use of multiple medications to manage symptoms, and barriers to care experienced by people with disabilities.^{56,57} The intersection of maternal disability and substance use (in particular non-medical opioid use) is an emerging area of research. People with different types of disabilities frequently report chronic pain directly attributable to or as a secondary condition to disability, and are commonly treated with analgesics including opioids and multiple medications.⁵⁸⁻⁶⁰ Pregnant people with disabilities are twice as likely as those without disabilities to use opioids in pregnancy.^{59,61,62} Further, they are more likely to be prescribed higher doses and report non-prescription use, most commonly as a means to manage pain. These represent risk factors for drug toxicity.^{59,62}

Risk Factors Associated with Drug Toxicity in Pregnancy

Understanding the risk factors and circumstances surrounding drug toxicity is critical to developing appropriate preconception and perinatal supports to prevent maternal mortality. There is little information on risk factors for unintentional drug toxicity in pregnancy in Canada. Most of the data on this topic is from studies and maternal

mortality review committees conducted in the US. Patient, provider, community, and system level risk factors are described below.

Patient

Psychiatric conditions and substance use disorders are two commonly studied factors that increase the risk of drug toxicity in pregnancy.^{49,63-67} For example, a US Centers for Disease Control and Prevention maternal mortality review committee examined 102 substance-related pregnancy deaths from 6 states.⁶⁸ They found that substance use disorders contributed to 94%, psychiatric conditions contributed to 72%, and both substance use disorders and psychiatric conditions contributed to 66% of the reviewed deaths. Treatment discontinuation for psychiatric and substance use disorders were also identified as risk factors for drug toxicity in pregnancy.^{49,63,64} Conversely, longer durations of opioid agonist therapy in pregnancy, compared to not receiving opioid agonist therapy, have been associated with a decreased risk of non-fatal opioid overdose in pregnancy in people with opioid use disorder.⁶⁹

Type of drug used is an important determinant of drug toxicity. The reviewed studies identified opioids as the predominant drug class involved in toxicity deaths.^{1,7,27,66,67,70} In particular, there have been significant increases in deaths involving synthetic opioids such as fentanyl. Additionally, increases were noted in the contribution of methamphetamines and polysubstance use (e.g., combinations of synthetic opioids and stimulants, or benzodiazepines) to drug toxicity deaths.^{1,27,63,64,66,70} In a perinatal mortality review in Utah, 83% of drug toxicity deaths were attributed to polysubstance use,²⁷ and in New York State, more than 1 in 4 pregnant women with opioid use disorder were also diagnosed with cannabis use disorder and cocaine use disorder.²⁶

Other patient-level risk factors associated with drug toxicity in pregnancy included exposure to domestic violence, unmarried marital status, younger age (<35 years), low

levels of education, White race, residence in low income/deprived neighbourhoods, co-occurring chronic medical conditions, involvement in the criminal justice system, and a family history of substance use.^{49,63,65,67,70,71} The intersectional nature of these patient-level characteristics further compounds the risk of drug toxicity in pregnancy.⁷²

Provider

Provider-level risk factors include poor access to healthcare (including a primary care provider and low-barrier medications for opioid use disorder), absence of knowledge regarding evidence-based prenatal addiction treatment, and provider judgement/discrimination.^{63,64,73} For example, pregnant people with opioid use disorder in Ontario are less likely to have a regular primary care provider than people with short-term use of opioids for pain in pregnancy (23% vs. 62%).⁷⁴ Similarly, a US study found that pregnant people with opioid use disorder were 20% less likely than non-pregnant people to be accepted by a healthcare provider for treatment.⁷⁵

Community

Risk factors identified at the community-level include ease of access to unregulated and prescription drugs, potency of the unregulated drug supply, and lack of access to antidotes including naloxone.^{63,73} Temporal factors such as the COVID-19 pandemic have led to increases in drug toxicity in pregnancy.^{1,3} Social isolation, restrictive maternity care, delivery protocols, and harm reductive services, and gaps in mental health services during the COVID-19 pandemic had unintended consequences for people who use drugs, in addition to widening existing health and social disparities. These factors limited access to healthcare and harm reduction services, which contributed to increases in drug toxicity deaths.⁵

System

System-level and structural risk factors include stigma, discrimination, racism, colonization, poverty, fear of child welfare, lack of low-barrier accessible addiction treatment, and a lack of access to mental health care prevent pregnant people from seeking perinatal addiction care.^{63,65,73}

Treatment for Pregnant Patients with Substance Use

The Society of Obstetricians and Gynaecologists of Canada (SOGC) recommends universal screening for substance use among reproductive-aged women and pregnant people.⁷⁶ They also recommend harm reduction approaches, brief interventions, and referrals to community resources for further interventions, as appropriate.

Comprehensive care

Given the complex health and social needs of people with substance use in pregnancy and systemic and structural oppression, the SOGC and The American College of Obstetricians and Gynecologist recommend using comprehensive treatment models to support patients and families affected by substance use.^{76,77} These models address important barriers to care by offering several social and medical services (e.g., medical care, prenatal care, addiction treatment, parenting support) in a centralized location. Care may involve behavioral and psychosocial interventions and pharmacotherapy. Comprehensive treatment models are associated with positive outcomes, such as decreased substance use in pregnancy, increased prenatal care, a greater likelihood of retaining child custody, and improvements in maternal and infant health outcomes.^{78,79} Furthermore, it is important for healthcare practitioners/service providers to establish trusting therapeutic relationships with patients in an effort to deliver flexible, non-judgemental, and empathetic care.²⁴ Pharmacotherapy specific to different substance disorders are briefly described below.

Pharmacotherapy

Alcohol Use Disorder

Naltrexone and acamprosate are approved medications for the treatment of alcohol use disorder. Naltrexone is a mu opioid receptor antagonist that has been shown to reduce heavy drinking.⁸⁰ There are no studies on the use of naltrexone in pregnant people with alcohol use disorder. Acamprosate has also been shown to reduce returning to drinking. There is insufficient human data to conclude about safety in pregnancy.⁸¹ The potential risks associated with the use of naltrexone and acamprosate in pregnancy should be weighed against the known risks of alcohol use.

Cannabis Use Disorder

There are no current pharmacotherapies for cannabis use disorder in pregnancy. The SOGC recommends that healthcare providers advise patients to abstain from cannabis use in pregnancy.⁷⁶

Opioid Use Disorder

The standard of care for the treatment of opioid use disorder in pregnancy, as recommended by the SOGC, is opioid agonist therapy (i.e., methadone, buprenorphine, or slow-release oral morphine). Opioid agonist therapy suppresses cravings, minimizes withdrawal, and prevents recurrent opioid use.⁷⁶ Compared with untreated unregulated opioid use in pregnancy, opioid agonist therapy is associated with decreased substance use, criminal activity, and mortality, improved treatment retention, prenatal care, maternal and infant outcomes (e.g., longer gestation, higher birth weights), and higher rates of retention of child custody.^{76,82,83} Naloxone is the recommended antidote for opioid overdose in pregnancy.⁸⁴

Physiologic changes that occur in pregnancy can impact drug disposition, which in turn, may necessitate modifications in dosing of methadone and buprenorphine.⁸⁵

Pregnancy-associated alterations include increased total body water and plasma volume (effect on volume of drug distribution), increased glomerular filtration rate (increased renal clearance), and changes in enzymes responsible for drug metabolism (modifications in hepatic metabolism). Most of these physiologic changes intensify as pregnancy progresses. For example, both methadone and buprenorphine are dependent on hepatic metabolism via cytochrome (CYP) 450 enzymes; CYP2B6 and 3A4 (methadone) and CYP3A4 (buprenorphine). Both CYP2B6 and CYP3A4 are upregulated during pregnancy, particularly in the third trimester. Some people will require increasing doses of methadone or buprenorphine as pregnancy progresses due to increased hepatic metabolism and renal drug clearance.⁸⁶⁻⁸⁸

Stimulant Use Disorder

There is no approved pharmacotherapy for stimulant use disorder in pregnancy.⁴²

Recommended management includes psychosocial therapies, (cognitive-behavioural therapy), contingency management techniques, and multidisciplinary care.⁷⁶

Knowledge Gaps

Limited Canadian and Ontario-specific data exist on prenatal substance use and unintentional drug toxicity deaths in pregnancy. Consequently, there is a lack of information on substance use patterns in pregnancy (e.g., type of substance, timing, frequency, and dose), as well as characteristics, risk factors, and circumstances associated with drug toxicity deaths in pregnancy. High-quality data is needed to inform prevention efforts, treatment and interventions, and programs and services to support patients and families affected by substance use. The SOGC is currently leading an initiative to develop a national confidential enquiry surveillance system to accurately record maternal deaths in Canada to address this knowledge gap.⁸⁹

Limitations

There are several limitations with the available literature on perinatal substance use and drug toxicity deaths in pregnancy. First, drug toxicity deaths in pregnancy may be systematically under reported due to a lack of standard reporting mechanisms. Second, perinatal deaths are rare, and standard definitions (i.e., pregnancy-associated, pregnancy-related deaths) typically include deaths during pregnancy and one-year after birth. Current data may be more reflective of postpartum risks because most pregnancy-associated deaths occur in the late postpartum period. Third, substance-related deaths are not always described by intent. Some studies combine intentional, unintentional, and undetermined substance-related deaths. This can potentially lead to misclassification of the intent and circumstances surrounding substance-related deaths. Fourth, low event rates (though positive) mean that sample sizes may be insufficient for more complex statistical analyses of risk factors. As a result, most studies on this topic are descriptive or ecological analyses. Fifth, an important methodological challenge when investigating substance use in pregnancy is residual confounding. Observed effects may be confounded by polysubstance use and intersecting socio-environmental and clinical factors. Sixth, many studies use administrative data to identify substance use in pregnancy. These data reflect users of the healthcare system, rely on accuracy of diagnostic coding, and may therefore, under-estimate substance use. In addition, studies that rely on maternal self-report may under-estimate the true prevalence of substance use. Patients may be less likely to report use due to social desirability, recall bias, and fear of stigma, discrimination, and involvement of child welfare. Lastly, race and ethnicity are not routinely collected in administrative data in Canada. As a result, little is known about the impact of patient race and experiences of racism on drug toxicity. Nevertheless, health administrative data are an important source of population-based data on prenatal substance use, are widely available, and highly generalizable.

Future Direction

Provincial health and demographic administrative data can be used to address critical knowledge gaps and limitations with existing research in Ontario. Two studies using administrative data from Ontario are underway to address knowledge gaps in pregnancy-associated mortality. The first examines trends and characteristics of pregnancy-associated opioid toxicity and opioid-related and all-cause mortality from 2013 to 2022. The second study examines the risk, and associated risk factors, of opioid toxicity within one-year of pregnancy in people with and without disabilities. Concurrently, as mentioned above, a harmonized national system to collect standardized information on maternal deaths from each province/territory is being developed,⁸⁹ in addition to a Canada-wide survey system that will collect information on pregnancy-related morbidity.⁹⁰

Table 1. Characteristics and Risk Factors for Drug Toxicity in Pregnancy

Reference	Time period	Location	Outcome	Main Findings	Characteristics or Risk Factors
PHAC ⁷	2009-2022	Canada	Fatal and non-fatal substance-related poisonings in pregnancy	419 substance-related poisoning hospitalizations 63% increase from 2020 to 2021 Half unintentional Opioids involved in 71-89% in 2021 and 2022	30% of substance-related poisoning hospitalizations were in 26-30yo
Jago et al. ⁴⁹	1998-2015	Alberta, Canada	Pregnancy-associated death from suicide, traumatic death, drug toxicity	206 deaths 24 (12%) attributed to drug toxicity	All drug toxicity deaths <35yo 83% smoked cigarettes in pregnancy 22% had a psychiatric disorder 28% were taking psychiatric medications
Gemmill et al. ⁷⁰	2007-2016	US, 22 states and DC	Pregnancy-associated mortality	Pregnancy-associated mortality rate involving opioids increased from 1.3 to 4.2 per 100,000 live births over the study period Deaths involving opioids due to heroin or synthetic opioids increased from 17% in 2007 to 78% in 2016	Nearly all overdoses involved opioids Most involved polysubstance use

Reference	Time period	Location	Outcome	Main Findings	Characteristics or Risk Factors
Mangla et al. ⁶³	NA	US	Pregnancy-associated self-harm deaths, including overdose deaths	Reviewed state prevalence of pregnancy-associated deaths	Psychiatric diagnoses Discontinuation of psychiatric medication SUD Intimate partner violence Older age Native American Opioid use Stigma and fear of child welfare as barriers to care Lack of treatment options Lack of access to OAT Chronic medical conditions Family history of substance use Opiate prescription after c-section Delivery complications Ease of accessibility to unregulated and prescription drugs
Bruzelius et al. ¹	2017-2020	US	Pregnancy-associated drug overdose mortality	Pregnancy-associated drug overdose death rate increased from 6.6 to 11.9 per 100,000 live births from 2017 to 2020 (increase of 81%). Drug overdose mortality peaked in 2020 Increases in deaths involving fentanyl, other synthetic opioids, and psychostimulants (e.g., methamphetamine, cocaine)	Fentanyl/synthetic opioids Stimulants Polysubstance use COVID-19
Margerison et al. ⁹¹	2010-2019	US	Pregnancy-associated deaths due to drugs, suicide, and homicide	11.4% of deaths due to drugs (10.5% pregnancy, 17% late postpartum [43-365 days post birth]) Pregnancy-associated drug related mortality rate was 4.7/100,000 live births. The rate increased from 2.7 to 7.8 per 100,000 live births from 2010 to 2019 (190% increase) 34% of deaths due to drugs occurred in pregnancy, 19.2% occurred in the first 42 days after birth, and 46.4% from 43-365 days after birth.	American Indian or Alaska Native at highest risk of drug-related death Most common in people 35y+ Rates most pronounced in 2020, coinciding with COVID-19

Reference	Time period	Location	Outcome	Main Findings	Characteristics or Risk Factors
Margerison et al. ³	2018-2020	US	Pregnancy-associated deaths	Pregnancy-associated drug related mortality rate: 7.1, 8.7, 13.4 per 100,000 livebirths in 2018, 2019, 2020, respectively 21% increase from 2018 to 2019 55% increase from 2019 to 2020	COVID-19
CDC ⁶⁸	2015-2019	US, 6 states	Pregnancy-associated deaths	86% of pregnancy-associated deaths involved opioids SUD contributed to 94% of pregnancy-associated overdose deaths, mental illness (other than SUD) 72%, both SUD and mental illness (66%) 19% pregnant at time of death	80% White people 39% 25-29yo, 26% 30-34yo 70% High School education or less 65% on Medicaid
Austin et al. ⁶⁵	2018-2019	US, North Carolina	Pregnancy-associated deaths	15.1 deaths per 100,000 live births from unintentional opioid overdose Less than one-fourth (22.2%) of those who died by unintentional opioid-involved overdose had a history of SUD treatment	Characteristics of unintentional opioid-involved overdose deaths in pregnancy: 61% 25-34yo 75% White people 69% high school education or less 83% late postpartum 81% involved fentanyl, 42% heroin, cocaine 39%, alprazolam 19% 80% had a history of opioid misuse or unregulated opioid use 33% bystander present
Han et al. ⁷¹	2018-2021	US	Pregnancy-associated deaths	Pregnancy-associated mortality ratio for unintentional/undetermined drug toxicity significantly increased across study period and tripled in women 35-44yo	Compared to pregnant decedents (all-cause), pregnant overdose decedents were more likely to: Have less than high school education Die outside of the home and healthcare settings Unmarried American born Reside in a low-income/deprived neighbourhood

Reference	Time period	Location	Outcome	Main Findings	Characteristics or Risk Factors
Campbell et al. ⁶⁴	NA	Primarily US	Pregnancy-associated deaths from homicide, suicide, overdose	Almost all overdose deaths involved more than 1 drug	Intimate partner violence Overprescribing of opioids Use of synthetic opioids and heroin Combination of opioids and benzodiazepines or alcohol Undiagnosed SUD Not receiving treatment for SUD Lack of access to SUD Psychiatric condition Chronic pain Witnessed an overdose Discrimination/stigma
Metz et al. ⁶⁶	2004-2012	US, Colorado	Pregnancy-associated deaths from self-harm	Accidental overdose: 5 per 100,000 live births Opioids were the most detected drugs in pregnancy-associated decedents	Psychiatric condition Domestic violence Gravidity 4+ Unemployed
Kountanis et al. ⁶⁷	2008-2018	US, Michigan	Pregnancy-related and pregnancy-associated deaths	3 most common drugs identified on toxicology reports: prescription opioids, heroin, cocaine 71% had a history of SUD >70% had a psychiatric condition, 48% had 2+ psychiatric conditions (only 35% had documented medication) 44% received inadequate prenatal care 30% had chronic pain 33% had prescriptions for both opioids and benzodiazepines at the time of death	Single marital status Intimate partner violence Psychiatric condition History of suicide attempt SUD Chronic pain Loss of child custody Multiparous Medicaid White
Smid et al. ⁷³	NA	NA	Review	Under-recognition of substance use among pregnant women is a significant contributing factor in women's deaths	Lack of SUD treatment Systemic shame and stigma Lack of provider knowledge of evidence-based treatment Lack of accessible SUD and mental illness treatment Loss of insurance

Reference	Time period	Location	Outcome	Main Findings	Characteristics or Risk Factors
Smid et al. ²⁷	2005-2014	US, Utah	Pregnancy-associated death due to drugs (intentional and unintentional)	Drug-induced pregnancy-associated mortality ratio increased 200%, from 3.9 to 11.7 per 100,000 live births from 2005 to 2014. Most identified deaths occurred in the late postpartum period. Most common cause of pregnancy-associated death was drug-induced death.	Drug-induced deaths were attributed to opioids (n=27/35, 77%), prescription opioids (n=21/35, 60%) and polysubstance use (n=29/35, 83%).
Howard et al. ²	2019-2020	US	All-cause and cause specific mortality, drug poisoning	321 drug poisoning pregnancy-associated deaths (8.6 per 100,000 live births) in 2019 and 442 (12.2 per 100,000 live births) in 2020. This corresponded to a rate ratio (comparing 2020 to 2019) of 1.42 (95% CI 1.22-1.63)	American Indian or Alaska Native people were 3 times more likely than White people to die from drugs

Abbreviations: SUD, substance use disorder; CI, confidence interval.

Maternal death was defined as a death during pregnancy or within 42 days of its termination, regardless of duration, for any cause related or aggravated by pregnancy.

Pregnancy-associated death was defined as a death during or within one year of pregnancy, regardless of the cause.

Pregnancy-related death was defined as a death during pregnancy or within one year of the end of pregnancy from a pregnancy complication, a chain of events initiated by pregnancy, or the aggravation of an unrelated condition by the physiologic effects of pregnancy.

Definitions

Maternal death – death of a woman during pregnancy or within 42 days of its termination, regardless of duration, for any cause related or aggravated by pregnancy.

Pregnancy-associated death - A death during or within one year of pregnancy, regardless of the cause.

Pregnancy-related death - A death during pregnancy or within one year of the end of pregnancy from a pregnancy complication, a chain of events initiated by pregnancy, or the aggravation of an unrelated condition by the physiologic effects of pregnancy.

References

1. Bruzelius E, Martins SS. US Trends in Drug Overdose Mortality Among Pregnant and Postpartum Persons, 2017-2020. *JAMA*. 2022;328(21):2159-2161.
2. Howard JT, Perrotte JK, Leong C, Grigsby TJ, Howard KJ. Evaluation of All-Cause and Cause-Specific Mortality by Race and Ethnicity Among Pregnant and Recently Pregnant Women in the US, 2019 to 2020. *JAMA Network Open*. 2023;6(1):e2253280-e2253280.
3. Margerison CE, Wang X, Gemmill A, Goldman-Mellor S. Changes in pregnancy-associated deaths in the US during the COVID-19 pandemic in 2020. *JAMA network open*. 2023;6(2):e2254287-e2254287.
4. Collier AY, Molina RL. Maternal Mortality in the United States: Updates on Trends, Causes, and Solutions. *Neoreviews*. Oct 2019;20(10):e561-e574. doi:10.1542/neo.20-10-e561
5. Gomes T MR, Kolla G, Leece P, Bansan S, Besharah J, Cahill T, Campbell T, Fritz A, Munro C, Toner L, Watford J on behalf of the Ontario Drug Policy Research Network, Office of the Chief Coroner for Ontario and Ontario Agency for Health Protection and Promotion (Public Health Ontario),. Changing circumstances surrounding opioid-related deaths in Ontario during the COVID-19 pandemic. Toronto, ON: Ontario Drug Policy Research Network; 2021.
6. Zipursky J, Juurlink DN. Opioid use in pregnancy: An emerging health crisis. *Obstet Med*. Dec 2021;14(4):211-219. doi:10.1177/1753495x20971163
7. Public Health Agency of Canada. Substance-related poisonings hospitalizations among people who are pregnant in Canada. Public Health Agency of Canada. <https://www.canada.ca/en/health-canada/services/opioids/data-surveillance-research/substance-related-poisonings-hospitalizations-people-pregnant-canada.html>
8. Turner SD, Gomes T, Camacho X, et al. Neonatal opioid withdrawal and antenatal opioid prescribing. *CMAJ open*. 2015;3(1):E55.
9. MacDonald M, Cheng C, Wang T, et al. Trends in varying modes of drug use in opioid toxicity deaths in Ontario from 2017 to 2021. *Int J Drug Policy*. Sep 22 2023;104197. doi:10.1016/j.drugpo.2023.104197
10. Humphries A, Simcox K, Howell B. A review of the literature: How does prenatal opioid exposure impact placental health and fetal brain development? *Dev Psychobiol*. Apr 2023;65(3):e22378. doi:10.1002/dev.22378
11. Corsi DJ, Walsh L, Weiss D, et al. Association Between Self-reported Prenatal Cannabis Use and Maternal, Perinatal, and Neonatal Outcomes. *Jama*. Jul 9 2019;322(2):145-152. doi:10.1001/jama.2019.8734
12. Zhang Y, Gong F, Liu P, He Y, Wang H. Effects of Prenatal Methamphetamine Exposure on Birth Outcomes, Brain Structure, and Neurodevelopmental Outcomes. *Dev Neurosci*. 2021;43(5):271-280. doi:10.1159/000517753

13. Camden A, Ray JG, To T, Gomes T, Bai L, Guttman A. Prevalence of Prenatal Opioid Exposure in Ontario, Canada, 2014-2019. *JAMA Network Open*. 2021;4(2):e2037388-e2037388. doi:10.1001/jamanetworkopen.2020.37388
14. Camden A, To T, Ray JG, Gomes T, Bai L, Guttman A. Categorization of Opioid Use Among Pregnant People and Association With Overdose or Death. *JAMA Netw Open*. May 2022;5(5):e2214688. doi:10.1001/jamanetworkopen.2022.14688
15. Metz VE, Brown QL, Martins SS, Palamar JJ. Characteristics of drug use among pregnant women in the United States: Opioid and non-opioid illegal drug use. *Drug and alcohol dependence*. 2018;183:261-266.
16. Corsi DJ, Hsu H, Weiss D, Fell DB, Walker M. Trends and correlates of cannabis use in pregnancy: a population-based study in Ontario, Canada from 2012 to 2017. *Can J Public Health*. Feb 2019;110(1):76-84. doi:10.17269/s41997-018-0148-0
17. Smid MC, Metz TD, Gordon AJ. Stimulant Use in Pregnancy: An Under-recognized Epidemic Among Pregnant Women. *Clin Obstet Gynecol*. Mar 2019;62(1):168-184. doi:10.1097/grf.0000000000000418
18. Bowie AC, Werler MM, Velez MP, et al. Prescribed opioid analgesics in early pregnancy and the risk of congenital anomalies: a population-based cohort study. *Cmaj*. Feb 7 2022;194(5):E152-e162. doi:10.1503/cmaj.211215
19. Brogly SB, Velez MP, Werler MM, Li W, Camden A, Guttman A. Prenatal Opioid Analgesics and the Risk of Adverse Birth Outcomes. *Epidemiology*. May 1 2021;32(3):448-456. doi:10.1097/ede.0000000000001328
20. Corsi DJ, Hsu H, Fell DB, Wen SW, Walker M. Association of Maternal Opioid Use in Pregnancy With Adverse Perinatal Outcomes in Ontario, Canada, From 2012 to 2018. *JAMA Netw Open*. Jul 1 2020;3(7):e208256. doi:10.1001/jamanetworkopen.2020.8256
21. Luke S, Hobbs AJ, Smith M, et al. Cannabis use in pregnancy and maternal and infant outcomes: A Canadian cross-jurisdictional population-based cohort study. *PLoS One*. 2022;17(11):e0276824. doi:10.1371/journal.pone.0276824
22. Yazdy MM, Desai RJ, Brogly SB. Prenatal Exposures and Short and Long Term Developmental Outcomes: Prescription Opioids in Pregnancy and Birth Outcomes: A Review of the Literature. *Journal of pediatric genetics*. 2015;4(2):56. doi:10.1055/s-0035-1556740
23. Schmidt R, Wolfson L, Stinson J, Poole N, Greaves L. Mothering and Opioids: Addressing Stigma and Acting Collaboratively. *Vancouver, BC: Centre of Excellence for Women's Health Retrived from: <http://bccewh.bc.ca/wp-content/uploads/2019/11/CEWH-01-MO-Toolkit-WEB2.pdf>*. 2019;
24. Wolfson L, Schmidt RA, Stinson J, Poole N. Examining barriers to harm reduction and child welfare services for pregnant women and mothers who use substances using a stigma action framework. *Health Soc Care Community*. May 2021;29(3):589-601. doi:10.1111/hsc.13335

25. Aflaki K, Ray JG. How other countries can improve Canada's maternal mortality statistics. *Obstet Med*. Dec 2023;16(4):211-216. doi:10.1177/1753495x231178405
26. Shen Y, Lo-Ciganic WH, Segal R, Goodin AJ. Prevalence of substance use disorder and psychiatric comorbidity burden among pregnant women with opioid use disorder in a large administrative database, 2009-2014. *J Psychosom Obstet Gynaecol*. Feb 18 2020:1-7. doi:10.1080/0167482x.2020.1727882
27. Smid MC, Stone NM, Baksh L, et al. Pregnancy-Associated Death in Utah: Contribution of Drug-Induced Deaths. *Obstet Gynecol*. Jun 2019;133(6):1131-1140. doi:10.1097/aog.0000000000003279
28. Tran EL, England LJ, Park Y, Denny CH, Kim SY. Systematic Review: Polysubstance Prevalence Estimates Reported during Pregnancy, US, 2009-2020. *Matern Child Health J*. Mar 2023;27(3):426-458. doi:10.1007/s10995-023-03592-w
29. Lange S, Quere M, Shield K, Rehm J, Popova S. Alcohol use and self-perceived mental health status among pregnant and breastfeeding women in Canada: a secondary data analysis. *Bjog*. May 2016;123(6):900-9. doi:10.1111/1471-0528.13525
30. Public Health Agency of Canada. *What Mothers Say: The Canadian Maternity Experiences Survey*. 2009. <https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/rhs-ssg/pdf/survey-eng.pdf>
31. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Snapshots: maternal health snapshot: Alcohol exposure during pregnancy. . King's Printer for Ontario. Accessed 01-31-2024, <https://www.publichealthontario.ca/en/Data-and-Analysis/Reproductive-and-Child-Health/Maternal-Health>
32. Potter A, Weinstock DM. *High time: The legalization and regulation of cannabis in Canada*. McGill-Queen's Press-MQUP; 2019.
33. Myran DT, Roberts R, Pugliese M, et al. Acute care related to cannabis use during pregnancy after the legalization of nonmedical cannabis in Ontario. *Canadian Medical Association Journal*. 2023;195(20):E699-E708. doi:10.1503/cmaj.230045
34. Brogly SB, Turner S, Lajkosh K, et al. Infants Born to Opioid-Dependent Women in Ontario, 2002-2014. *J Obstet Gynaecol Can*. Mar 2017;39(3):157-165. doi:10.1016/j.jogc.2016.11.009
35. Nechuta S, Mukhopadhyay S, Golladay M, Rainey J, Krishnaswami S. Trends, patterns, and maternal characteristics of opioid prescribing during pregnancy in a large population-based cohort study. *Drug Alcohol Depend*. Jan 26 2022;233:109331. doi:10.1016/j.drugalcdep.2022.109331
36. Sujan AC, Quinn PD, Rickert ME, et al. A nation-wide Swedish study of opioid analgesic prescribing patterns during pregnancy and associated preexisting mental health conditions. *J Matern Fetal Neonatal Med*. Jan 13 2021:1-7. doi:10.1080/14767058.2021.1875436

37. Smith MV, Costello D, Yonkers KA. Clinical correlates of prescription opioid analgesic use in pregnancy. *Matern Child Health J.* Mar 2015;19(3):548-56. doi:10.1007/s10995-014-1536-6
38. Whiteman VE, Salemi JL, Mogos MF, Cain MA, Aliyu MH, Salihu HM. Maternal opioid drug use during pregnancy and its impact on perinatal morbidity, mortality, and the costs of medical care in the United States. *Journal of pregnancy.* 2014;2014:906723. doi:10.1155/2014/906723 [doi]
39. Arnaudo CL, Andraka-Christou B, Allgood K. Psychiatric co-morbidities in pregnant women with opioid use disorders: Prevalence, impact, and implications for treatment. *Current addiction reports.* 2017;4(1):1-13.
40. Kozhimannil KB, Graves AJ, Levy R, Patrick SW. Nonmedical use of prescription opioids among pregnant US women. *Women's Health Issues.* 2017;27(3):308-315.
41. Holbrook AM, Baxter JK, Jones HE, et al. Infections and obstetric outcomes in opioid-dependent pregnant women maintained on methadone or buprenorphine. *Addiction.* 2012;107:83-90.
42. Turner S, Nader M, Lurie E. A contingency management approach for treatment of methamphetamine use disorder and human immunodeficiency virus antiretroviral treatment adherence in pregnancy to prevent mother-to-child transmission: a case report. *Journal of Medical Case Reports.* 2022/04/27 2022;16(1):165. doi:10.1186/s13256-022-03391-x
43. Popova S, Dozet D, O'Hanlon G, Temple V, Rehm J. Maternal alcohol use, adverse neonatal outcomes and pregnancy complications in British Columbia, Canada: a population-based study. *BMC Pregnancy Childbirth.* Jan 22 2021;21(1):74. doi:10.1186/s12884-021-03545-7
44. Sujan AC, Alexeeff SE, Slama NE, et al. Agreement Between Self-reports and Urine Toxicology Measures of Illicit Methamphetamine and Cocaine Use During Early Pregnancy. *J Addict Med.* Jan-Feb 01 2024;18(1):28-32. doi:10.1097/adm.0000000000001230
45. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Snapshots: maternal health snapshot: Drug exposure during pregnancy. King's Printer for Ontario. Accessed 01-29-2024, <https://www.publichealthontario.ca/en/Data-and-Analysis/Reproductive-and-Child-Health/Maternal-Health>
46. Statistics Canada. Table 13-10-0756-01 Number of maternal deaths and maternal mortality rates for selected causes. 2024.
47. Boutin A, Cherian A, Liauw J, et al. Database Autopsy: An Efficient and Effective Confidential Enquiry into Maternal Deaths in Canada. *J Obstet Gynaecol Can.* Jan 2021;43(1):58-66.e4. doi:10.1016/j.jogc.2020.06.026
48. Aflaki K, Vigod SN, Sprague AE, et al. Maternal Deaths Using Coroner's Data: A Latent Class Analysis. *J Obstet Gynaecol Can.* Jan 6 2024:102349. doi:10.1016/j.jogc.2024.102349

49. Jago CA, Crawford SG, Gill SJ, Gagnon L. Mental Health and Maternal Mortality-When New Life Doesn't Bring Joy. *J Obstet Gynaecol Can.* Jan 2021;43(1):67-73.e1. doi:10.1016/j.jogc.2020.06.016
50. Chiefs of Ontario & ICES. Mental Health and Addiction System Performance in Ontario First Nations (2009-2019). 2021.
51. Chiefs of Ontario and Ontario Drug Policy Research Network. Opioid use, related harms, and access to treatment among First Nations in Ontario, 2013-2019. Toronto, ON.: Chiefs of Ontario.; 2021.
52. Dooley J, Ryan G, Gerber Finn L, et al. Maternal opioid use disorder and neonatal abstinence syndrome in northwest Ontario: a 7-year retrospective analysis. *Can J Rural Med.* Spring 2018;23(2):39-44.
53. Allen L, Wodtke L, Hayward A, Read C, Cyr M, Cidro J. Pregnant and early parenting Indigenous women who use substances in Canada: A scoping review of health and social issues, supports, and strategies. *J Ethn Subst Abuse.* Mar 3 2022:1-31. doi:10.1080/15332640.2022.2043799
54. Jumah NA, Edwards C, Balfour-Boehm J, et al. Observational study of the safety of buprenorphine+naloxone in pregnancy in a rural and remote population. *BMJ Open.* Oct 31 2016;6(10):e011774. doi:10.1136/bmjopen-2016-011774
55. Carroll Chapman SL, Wu LT. Substance abuse among individuals with intellectual disabilities. *Res Dev Disabil.* Jul-Aug 2012;33(4):1147-56. doi:10.1016/j.ridd.2012.02.009
56. Saeed G, Brown HK, Lunskey Y, et al. Barriers to and facilitators of effective communication in perinatal care: a qualitative study of the experiences of birthing people with sensory, intellectual, and/or developmental disabilities. *BMC Pregnancy and Childbirth.* 2022/04/26 2022;22(1):364. doi:10.1186/s12884-022-04691-2
57. Tarasoff L, Lunskey Y, Welsh K, et al. Understanding and addressing the pregnancy care needs of women with disabilities in Ontario. *Journal of Obstetrics and Gynaecology Canada.* 2021/05/01/ 2021;43(5):663-664. doi:<https://doi.org/10.1016/j.jogc.2021.02.050>
58. Tarasoff LA, Lunskey Y, Chen S, et al. Preconception health characteristics of women with disabilities in Ontario: a population-based, cross-sectional study. *Journal of Women's Health.* 2020;29(12):1564-1575.
59. Booth EJ, Kitsantas P, Min H, Pollack AZ. Disability and Opioids Among Pregnant Women. *Women's Reproductive Health.* 2022:1-16. doi:10.1080/23293691.2022.2150105
60. Lunskey Y, Modi M. Predictors of Psychotropic Polypharmacy Among Outpatients With Psychiatric Disorders and Intellectual Disability. *Psychiatr Serv.* Feb 1 2018;69(2):242-246. doi:10.1176/appi.ps.201700032
61. García MH, Petersen JM, Parker SE, Rubenstein E, Werler MM. Medication use during pregnancy among women with congenital physical disabilities. *Birth Defects Research.* 2022;114(14):785-796.

62. Richard CL, Love BL, Boghossian N, Hardin J, McDermott S. Are pregnant women with disability prescribed opioids more and at higher dosages than those without disability?: A retrospective cohort study of South Carolina Medicaid beneficiaries. *Disability and Health Journal*. 2022;15(2):101288.
63. Mangla K, Hoffman MC, Trumpff C, O'Grady S, Monk C. Maternal self-harm deaths: an unrecognized and preventable outcome. *Am J Obstet Gynecol*. Oct 2019;221(4):295-303. doi:10.1016/j.ajog.2019.02.056
64. Campbell J, Matoff-Stepp S, Velez ML, Cox HH, Laughon K. Pregnancy-Associated Deaths from Homicide, Suicide, and Drug Overdose: Review of Research and the Intersection with Intimate Partner Violence. *J Womens Health (Larchmt)*. Feb 2021;30(2):236-244. doi:10.1089/jwh.2020.8875
65. Austin AE, Naumann RB, DiPrete BL, Geary S, Proescholdbell SK, Jones-Vessey K. Pregnancy-associated homicide, suicide and unintentional opioid-involved overdose deaths, North Carolina 2018-2019. *Inj Prev*. Jan 9 2024;doi:10.1136/ip-2023-045112
66. Metz TD, Rovner P, Hoffman MC, Allshouse AA, Beckwith KM, Binswanger IA. Maternal Deaths From Suicide and Overdose in Colorado, 2004-2012. *Obstet Gynecol*. Dec 2016;128(6):1233-1240. doi:10.1097/aog.0000000000001695
67. Kountanis JA, Roberts M, Admon LK, Smith R, Cropsey A, Bauer ME. Maternal deaths due to suicide and overdose in the state of Michigan from 2008 to 2018. *Am J Obstet Gynecol MFM*. Feb 2023;5(2):100811. doi:10.1016/j.ajogmf.2022.100811
68. Centers for Disease Control and Prevention. Fact Sheet: Pregnancy-associated Overdose Deaths, 2015-2019.
69. Jarlenski M, Chen Q, Gao A, Rothenberger SD, Krans EE. Association of Duration of Methadone or Buprenorphine Use During Pregnancy With Risk of Nonfatal Drug Overdose Among Pregnant Persons With Opioid Use Disorder in the US. *JAMA Netw Open*. Apr 1 2022;5(4):e227964. doi:10.1001/jamanetworkopen.2022.7964
70. Gemmill A, Kiang MV, Alexander MJ. Trends in pregnancy-associated mortality involving opioids in the United States, 2007-2016. *Am J Obstet Gynecol*. Jan 2019;220(1):115-116. doi:10.1016/j.ajog.2018.09.028
71. Han B, Compton WM, Einstein EB, Elder E, Volkow ND. Pregnancy and Postpartum Drug Overdose Deaths in the US Before and During the COVID-19 Pandemic. *JAMA Psychiatry*. Nov 22 2023;doi:10.1001/jamapsychiatry.2023.4523
72. Knight M, Felker B, Patel A, Kotnis R, Kenyon S, Kurinczuk J. Saving Lives, Improving Mothers' Care Core Report-Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2019-21. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2023.
73. Smid MC, Schauburger CW, Terplan M, Wright TE. Early lessons from maternal mortality review committees on drug-related deaths-time for obstetrical providers to take the lead in addressing addiction. *Am J Obstet Gynecol MFM*. Nov 2020;2(4):100177. doi:10.1016/j.ajogmf.2020.100177

74. Camden A, To T, Gomes T, Ray J, Bai L, Guttmann A. Prenatal opioid exposure and well-child care in the first 2 years of life: population-based cohort study. *Arch Dis Child*. Sep 2023;108(9):754-761. doi:10.1136/archdischild-2022-325029
75. Phillippi JC, Schulte R, Bonnet K, et al. Reproductive-Age Women's Experience of Accessing Treatment for Opioid Use Disorder: "We Don't Do That Here". *Womens Health Issues*. Sep-Oct 2021;31(5):455-461. doi:10.1016/j.whi.2021.03.010
76. Ordean A, Wong S, Graves L. No. 349-Substance Use in Pregnancy. *Journal of Obstetrics and Gynaecology Canada*. 2017;39(10):922-937. e2. doi:10.1016/j.jogc.2017.04.028
77. American College of Obstetricians and Gynecologists. Committee Opinion No. 711: Opioid Use and Opioid Use Disorder in Pregnancy. *Obstet Gynecol*. Aug 2017;130(2):e81-e94. doi:10.1097/aog.0000000000002235
78. Ordean A, Kahan MJCFP. Comprehensive treatment program for pregnant substance users in a family medicine clinic. 2011;57(11):e430-e435.
79. Ordean A, Kahan M, Graves L, Abrahams R, Kim T. Obstetrical and neonatal outcomes of methadone-maintained pregnant women: a Canadian multisite cohort study. *Journal of Obstetrics and Gynaecology Canada*. 2015;37(3):252-257.
80. McPheeters M, O'Connor EA, Riley S, et al. Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis. *JAMA*. 2023;330(17):1653-1665. doi:10.1001/jama.2023.19761
81. Kelty E, Tran D, Lavin T, Preen DB, Hulse G, Havard A. Prevalence and safety of acamprosate use in pregnant alcohol-dependent women in New South Wales, Australia. *Addiction*. Feb 2019;114(2):206-215. doi:10.1111/add.14429
82. Fullerton CA, Kim M, Thomas CP, et al. Medication-assisted treatment with methadone: assessing the evidence. *Psychiatr Serv*. Feb 1 2014;65(2):146-57. doi:10.1176/appi.ps.201300235
83. Thomas CP, Fullerton CA, Kim M, et al. Medication-assisted treatment with buprenorphine: assessing the evidence. *Psychiatr Serv*. Feb 1 2014;65(2):158-70. doi:10.1176/appi.ps.201300256
84. Turner S, Allen VM, Carson G, et al. Guideline No. 443b: Opioid Use Throughout Women's Lifespan: Opioid Use in Pregnancy and Breastfeeding. *Journal of Obstetrics and Gynaecology Canada*. 2023/11/01/ 2023;45(11):102144. doi:<https://doi.org/10.1016/j.jogc.2023.05.012>
85. Pariente G, Leibson T, Carls A, Adams-Webber T, Ito S, Koren G. Pregnancy-Associated Changes in Pharmacokinetics: A Systematic Review. *PLoS Med*. Nov 2016;13(11):e1002160. doi:10.1371/journal.pmed.1002160
86. Bogen DL, Perel JM, Helsel JC, et al. Pharmacologic evidence to support clinical decision making for peripartum methadone treatment. *Psychopharmacology (Berl)*. Jan 2013;225(2):441-51. doi:10.1007/s00213-012-2833-7

87. Wolff K, Boys A, Rostami-Hodjegan A, Hay A, Raistrick D. Changes to methadone clearance during pregnancy. *Eur J Clin Pharmacol*. Nov 2005;61(10):763-8. doi:10.1007/s00228-005-0035-5
88. Concheiro M, Jones HE, Johnson RE, Choo R, Huestis MA. Preliminary buprenorphine sublingual tablet pharmacokinetic data in plasma, oral fluid, and sweat during treatment of opioid-dependent pregnant women. *Ther Drug Monit*. Oct 2011;33(5):619-26. doi:10.1097/FTD.0b013e318228bb2a
89. Cook JL, Sprague AE. Measuring Maternal Mortality in Canada: An Update on the Establishment of a Confidential Enquiry System for Preventing Maternal Deaths #savingmoms #savingbabies. *J Obstet Gynaecol Can*. Dec 2019;41(12):1768-1771. doi:10.1016/j.jogc.2019.07.018
90. Malhamé I, Knight M, D'Souza R. Initial Steps in Developing and Implementing a Canadian Obstetric Survey System (CanOSS) for Severe Maternal Morbidity. *Journal of Obstetrics and Gynaecology Canada*. 2022;44(6):637-638. doi:10.1016/j.jogc.2022.02.002
91. Margerison CE, Roberts MH, Gemmill A, Goldman-Mellor S. Pregnancy-Associated Deaths Due to Drugs, Suicide, and Homicide in the United States, 2010-2019. *Obstet Gynecol*. Feb 1 2022;139(2):172-180. doi:10.1097/aog.0000000000004649

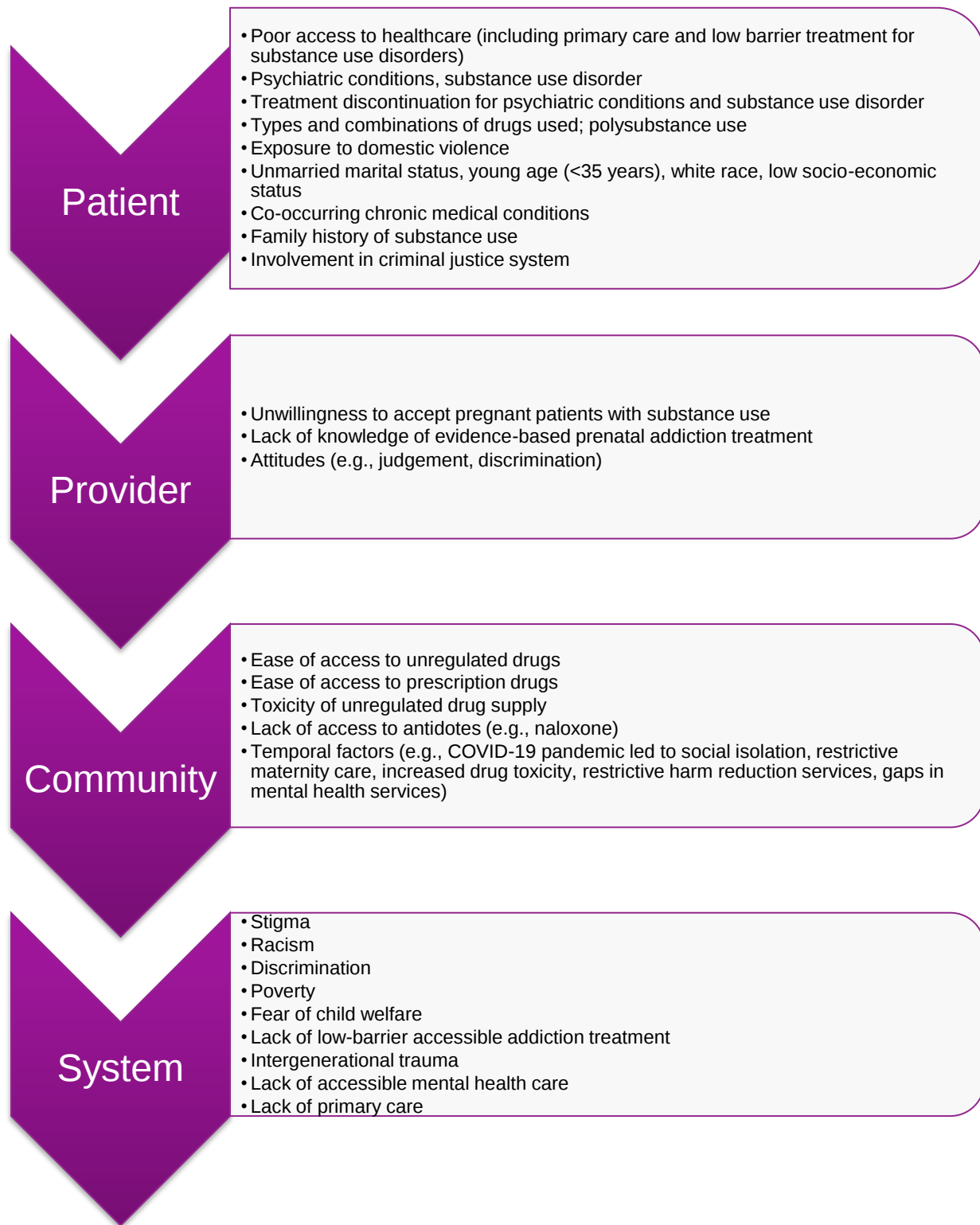
Appendix C: Case summaries

Case year	Brief summary
2013 - A	This individual was between the ages of 20 and 24 years and was 9 weeks pregnant. She had a long history of substance use disorder, with regular use of IV and intranasal opioids and cocaine, as well as a history of heroin, oxycodone, and hallucinogens. She had been on methadone maintenance therapy for a number of months. She had been diagnosed with a mental health disorder but was not on medication at the time of her death. The immediate cause of death was the combined effects of methadone and cyclobenzaprine.
2013 - B	This individual was between the ages of 25 and 29 years and was 6 weeks pregnant. She had a long history of substance use disorder including opioids, amphetamines, and cannabis, and had been on both methadone and buprenorphine, as well as completing a residential treatment program. The immediate cause of death was cardiorespiratory arrest due to fentanyl toxicity.
2017 - A	This individual was between the ages of 35 and 39 years and was 17 weeks pregnant. She had a long history of substance use disorder. She had been seen at an emergency department a few days prior to death for fentanyl toxicity. The immediate cause of death was cocaine toxicity.
2017 - B	This individual was between the ages of 30 and 34 years and was 30 weeks pregnant. She had a long history of polysubstance use including opioids, cocaine, alcohol, cannabis, and amphetamines. She had many years of methadone therapy. The immediate cause of death was a spontaneous intracranial bleed due to hypertension and methamphetamine toxicity.
2018 - A	This individual was between the ages of 30 and 34 years and was 7 weeks pregnant. They had a long history of substance use disorder. Opioid use began as a prescription for chronic pain, while long-term amphetamines had been prescribed for mental health disorders. The immediate cause of death was fentanyl toxicity.
2018 - B	This individual was between the ages of 25 and 29 years and was 32 weeks pregnant. She was unhoused and found unresponsive by shelter staff. Resuscitation was attempted by multiple parties but

	was unsuccessful. The immediate cause of death was acute mixed drug (fentanyl and methamphetamine) toxicity.
2019 - A	This individual was between the ages of 35 and 39 years and was 25 weeks pregnant. She had a long history of substance use disorder and had voluntarily entered multiple inpatient care units for treatment in the last 18 months of her life. The immediate cause of death was hypoxic-ischemic encephalopathy due to acute fentanyl toxicity.
2020 - A	This individual was between the ages of 30 and 34 years and was 15 weeks pregnant. She was known to use cocaine and methamphetamines and she had previous mental health diagnoses but was not using her prescribed medications at the time of death. The immediate cause of death was mixed drug toxicity (cocaine, fentanyl, and methamphetamines).
2020 - B	This individual was between the ages of 25 and 29 years and was 16 weeks pregnant. She had a known history of substance use disorder, including fentanyl and methamphetamines, and had recently been diagnosed with an autoimmune disorder. The immediate cause of death was fentanyl toxicity.
2021 - A	This individual was between the ages of 30 and 34 years and was 20 weeks pregnant. She was found unresponsive by a friend, and despite naloxone administration, was unable to be resuscitated. The immediate cause of death was fentanyl, methadone, cocaine, and possible etizolam toxicity.
2021 - B	This individual was between the ages of 25 and 29 years and was 25 weeks pregnant. She had a long-term history of substance use disorder, primarily amphetamines and fentanyl. She had been incarcerated for part of her pregnancy. The immediate cause of death was fentanyl, methamphetamine, and amphetamine toxicity.
2021 - C	This individual was between the ages of 25 and 29 years and was 36 weeks pregnant. She was precariously housed. She had attended an emergency department prior to her death for abdominal pain but had not returned for the follow-up appointment. The immediate cause of death was mixed intoxication of hydromorphone, amphetamines, and cocaine.
2021 - D	This individual was between the ages of 20 and 24 years and was 17 weeks pregnant. She had a long history of substance use disorder and had numerous emergency department visits arising from

	substance use. She had been incarcerated for part of her pregnancy. The immediate cause of death was fentanyl, cocaine, and methamphetamine toxicity.
2022 - A	This individual was between the ages of 30 and 34 years and was 4 weeks pregnant. She had a long history of stimulant use disorder and had tried inpatient rehabilitation and counseling. There was also a history of intimate partner violence. The immediate cause of death was acute fentanyl, cocaine, and methamphetamine toxicity.
2022 - B	This individual was between the ages of 25 and 29 years and was 22 weeks pregnant. She had a long history of polysubstance use disorder including fentanyl, heroin, and methamphetamines, and had previously experienced at least two near-fatal overdoses. The immediate cause of death was fentanyl, etizolam, and possible bromazolam and flubromazepam toxicity.
2022 - C	This individual was between the ages of 20 and 24 years and was 19 weeks pregnant. She had a long history of substance use disorder but had successfully used methadone during a previous pregnancy. There was also a history of intimate partner violence. The immediate cause of death was fentanyl, methadone, cocaine, and methamphetamine toxicity.
2022 - D	This individual was between the ages of 20 and 24 years and was 30 weeks pregnant. They had a long history of substance use disorder, as well as borderline personality disorder and substance-induced psychosis. There was also a history of intimate partner violence. The immediate cause of death was multi-drug toxicity including fentanyl, methamphetamine, amphetamine and cocaine.
2022 - E	This individual was between the ages of 30 and 34 years and was 6 weeks pregnant. She was insecurely housed and had a long history of polysubstance use disorder. She had been seen by her mental health support worker the day prior to her death. The immediate cause of death was fentanyl and cocaine toxicity.

Appendix D: Summary of Risk Factors for Drug Toxicity in Pregnancy



See Appendix B: Literature Review for more details and references